

A)

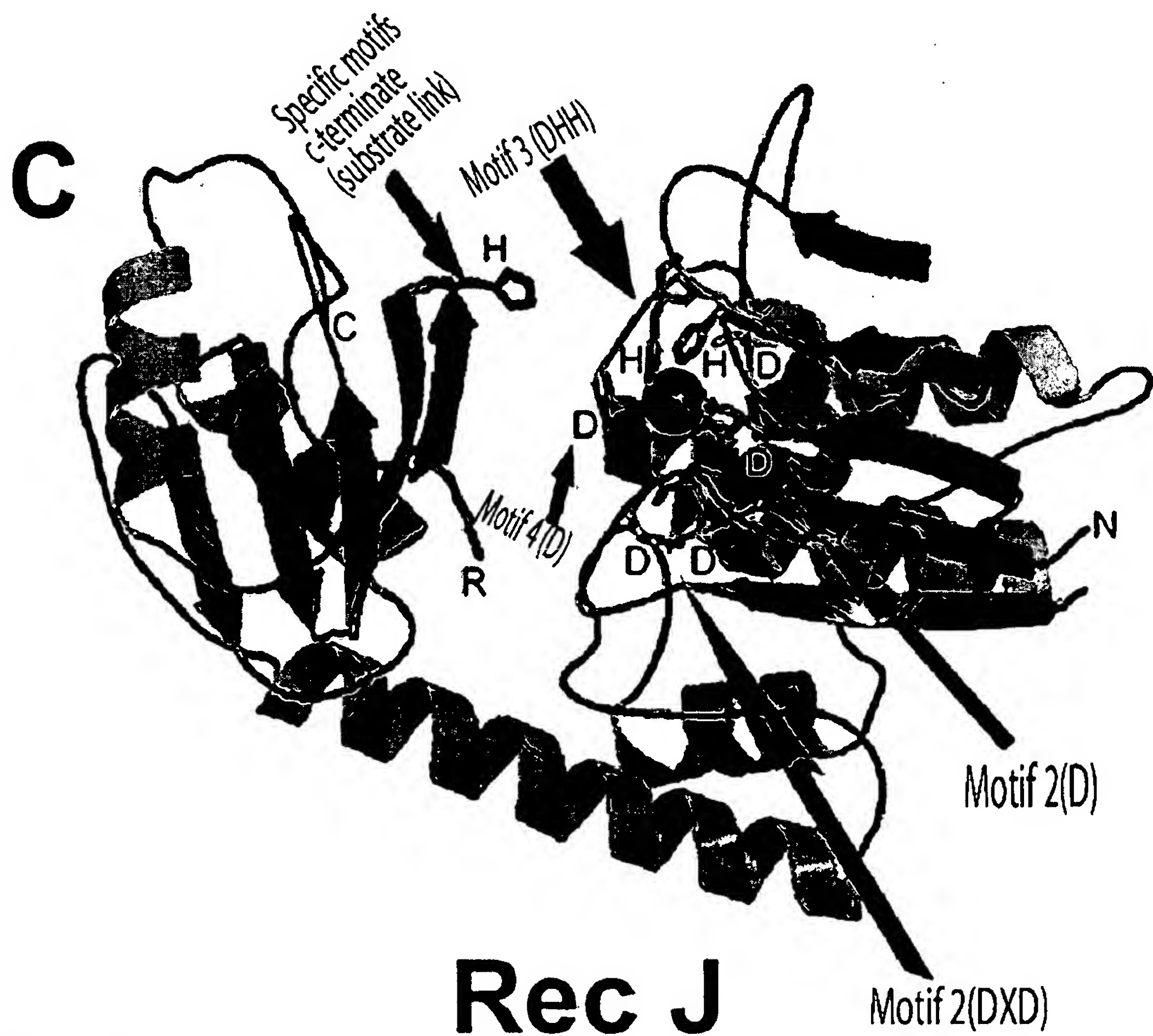
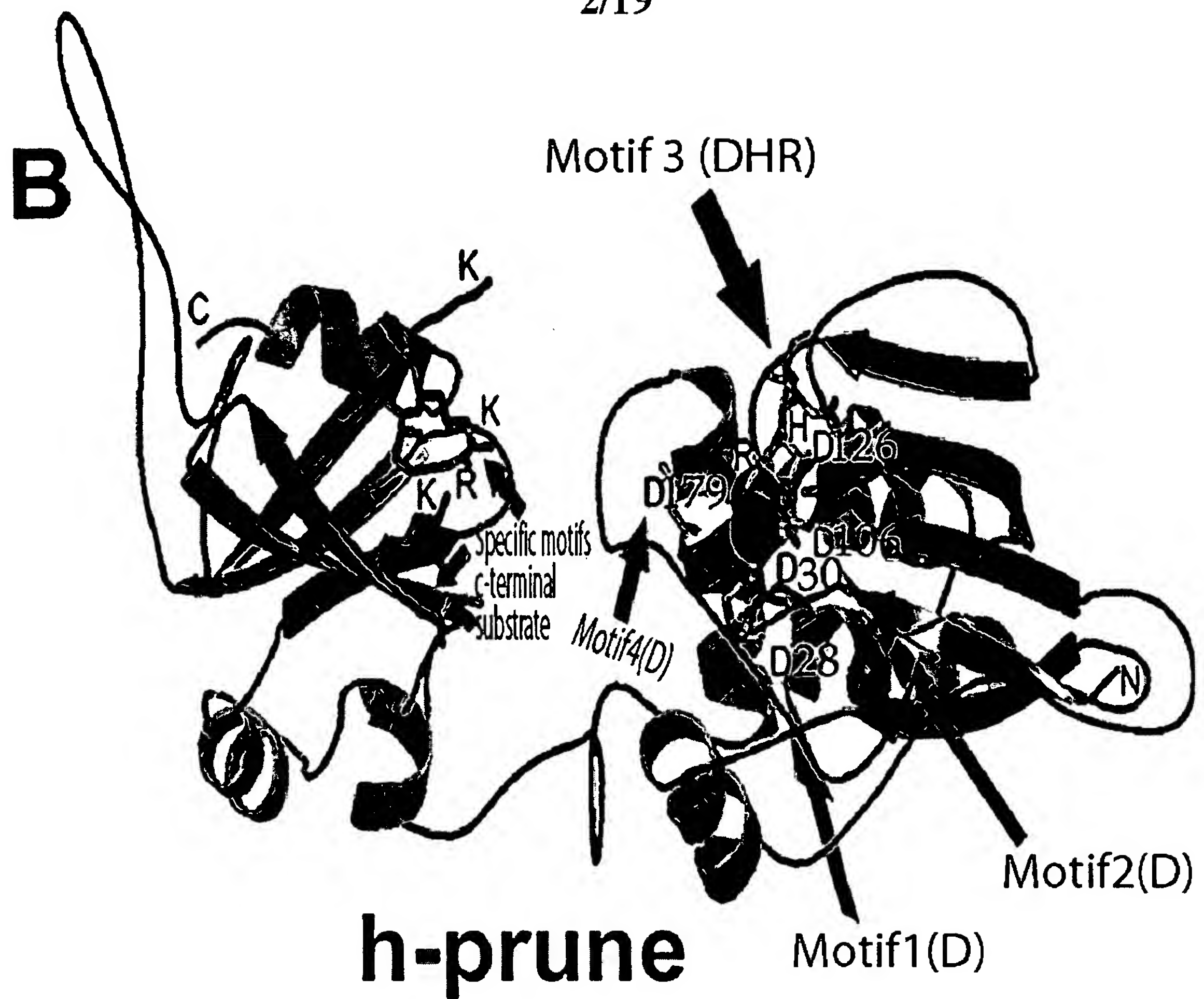
	Motif 1	Motif 2	Motif 3	Motif 4
Rv2837c_Mt	VGVCVHVHPDADTIGAGLALALVLDGCG [35]	VDLVVTVDPSPVDRLGALG [6]	RELVVDHHEASND [10]	SADSTTMVAEILDWAGKPIDPRVAHCIYAGLATDTGSPRWASV
s111253_Ssp	DLILCHQTAQDFDLVGAAGVGLAKLHPGSR [34]	IRSLYIVDQOQDRLGKAA [8]	RQVAIVDHEHNSP [11]	AVGASTTLIVEKLQRADISLSMVEASVMALGIHVDTGSLTFTQT
MGPA_Mg	IVIFPHVRPDPGCLGAQOQGLFHLIKANF [32]	EALAIIVDPANYKNRIELRE [7]	KAVLRIDHHPNED [11]	SYVACCEQIVEMATVAKWTIPPVAAATLLYIGIYTPDSNRFLYSNT
YTQI_Bs	IILHRHVRRPDPAYGSCQGLTEILRETY [30]	GALVIVQDTANQERIDDDR [4]	AKLMKIDHHPNED [13]	SVSEMIYELYLEGKEHGKWLNTKAAELIYAGIVGDTGRFLFPNT
AF2029_Af	LGIFTHDNPPDPSMSSAYALREIAKQFD [37]	YDAFAIVDSSGPGVNNIP [3]	DISIVDHEPAEK [10]	DVGATATILTEYIKELKITPSKILATALPFGIKSETDEFKRNTR
MJ0977_Mj	NKILIVTHIDTDGLTSRAILQKLAERLN [23]	YDLIFADLGSGQLKMIKE [11]	DKIILDHEQPEE [18]	GAEICGAGVSYLEPAKAINNDWIDLAKYAVLGAVGDIQNIIEGKLI
MJ1198_Mj	RPITIRHHADTDGYCGGIALEKAILPII [46]	LPLVLIDNGSTDEDIPAI [7]	IEVIVDHEHPGE [85]	KGRTYDREYLEKIALCMDFEAFYLRFMGKGIVDDILATNIKEP
HP1042_Hp	MQVYHLSHIDLDGYACQLVSKQFFKNIQ [27]	EFLILVSPDLNLNLEAEYL [13]	IQIQLIDHHISGK [19]	IVYEFLKKHYAILEPKNTTWLEPLVEMVNSVDINDTQGYGFELG
RecJ_Hi	QKIVIVGDFDADGATSTALSVALRQLG [31]	VQLLMTVDNGVSSFDGVAF [5]	IRVLVTDHELPEE [33]	LAVRAKFRELGIFTAETQPNFTDLDLVALGTIADVVPLDQNNR
RecJ_Hp	TEILVVGDDYDADGVISSAIMAKFFESLN [27]	APLITVDNGINAFEAARF [5]	YTLIITDHFCLHH [27]	LVAFYLCYGIHQLLGKEKSHSSELLCLAGVATIADMMPLTFFNR
RecJ_Ssp	EKVTIWGDFDADGITSTAVLWEGLGQFF [32]	TKLIVTQDTGSTNLDEIVY [5]	MDVIVTDHETLPD [27]	VAFKLVEALYNQYPTVPQQPLEDLDLVAIGLIADLVTLQGDCR
YYBQ_Bs	ILIFGHQNPDTDTICSAIAYADLKNKLG [36]	VNGVILVDHNERQQSIKDI [3]	QVLEVVDHERIAN [12]	PVGCTATIILNKMYKENNVKIEKEIAGLMLSAIISDLSLLPKSPTC
ICRA_Sg	ILVFGHQNPDSDAIGSSYAFAYLAREAY [38]	AEQVILTDEHNEFQQSVADI [3]	EVYGVVDHERVAN [12]	PVGSASSIVYRMFKEHSVAVSKEIAGLMLSLGLISDTLLLKSPPT
Y608_Mj	RYVVGHNKNPDTDSIASAIVLAYFLDCYP [31]	GKETILVDHSEKSSQSFDDL [3]	KLIAIDHFKVGL [19]	IAELYFKDAIDLIGGKKKELKPDLAGLLLSAIIISDTVLFPKSPTT
AF0756_Af	VYVVGHNKNPDTDSVCSAIAFAYLWNKWK [46]	GKKVALVDHSEKAQTVDGI [14]	EVVAIVDHHKIGD [12]	PVGCTATVIKLLFDKGTGVEIPKDIAGILLSSILSDTVIPKSATT
U60409_Lm	TVVQGNEGGMDSDSIVGCIYLAMLPDKQP [44]	QIAHNLVDIAALNASVWLY [2]	RVVGVVDHHPDEQ [11]	LRTVGSACTLVTELYREGGEDVVCPTLLTAPIVLDTVNPEPAQK
PPX1_Sc	TICVGNESADMDSIASAITYSYCQYIYN [62]	ELNSYLVNDNDTPKNLKNY [2]	NVVGIDHHPFDLQ [14]	SCSSLVFNYWYEKLQGDREVVMNIAPLLMGAILIDTSNMRRKVB
PRUNE_Dm	HLVMGNESQDLDSAVSAVTLAFVYAQRH [48]	DVNVLVDHHSVPLAPNVT [1]	NVTEILDHHPLED [18]	SVGSCATLVAQRYLAEDQPRSTSVAQLLHATIVLDVINPAPAAK
h-prune.1_Hs	HVVLGNEAQLDSTVSALALAFYLAKT [52]	QLTLILVDHHILSKSDTAL [2]	AVAENVDRHPREP [12]	LVGSCATLVTERILQGAPEILDRTAALLHGTIILDCVNMMDLKIG

	Specific motifs	GIs		
Rv2837c_Mt	[107] TVNLAAVASGFGGGHRLAAGYTTGS	1648883	Family 1	
sl11253_Ssp	[123] DTDLTQLLEPYGGGHAQAAA VNLRDV	1653244		
MGPA_Mg	[102] GINVRDIAIKYGGGGHNNASGAIITNK	1045875		
YTQI_Bs	[103] GPVINGLARKYNGGGHPLASGASIYSW	2293259		
AF2029_Af	[102] EVLRRAFGDVSGGHAHAAGAQIPLG	2648507		
MJ0977_Mj	[254] AIKYASEKVGSGGCHKFACGAYIPDN	2128614		
MJ1198_Mj	[109] QLMEEIPEASLDGGGHECAGSLKFVEG	2128720		
HP1042_Hp	[137] CDVCELSQCMFCNGGHRNASGGKIDGF	2314198		
RecJ_Hi	[168] RIHSQHPNMILKFGGHAMAAGLSIREE	1172895		
RecJ_Hp	[155] DALNGVSSLLLYGGHRQACGLSVEKN	2313437		
RecJ_Ssp	[165] ALLHSQRHMLGFGGHPFAAGLSPLD	1652638		
YYBQ_Bs	[31] DLSKKTVEELISLDAKEFTLG [ 75]	TALLKGVVSRKKQVVPVLT	586817	Family 2
ICRA_Sg	[31] NLASKSAEELIDIDAKTFELN [ 75]	HAPLAGAVSRKKQVVPQLTE	1743856	
MJ0608_Mj	[32] VVGKLKPEEIIINMDFKNFDEN [ 74]	SVFLEGVMSRKKQVPPLE	1591318	
AF0756_Af	[32] AVDDLTAMDIIRDYKDFDMS [ 75]	SVWLDGVMSRKKQVPPLEK	11498362	
L2759.9_Lm	[36] DVLALSVPQILRRDYKQFSFK [105]	YSLSDPSISRKK-LVPALSE	1407725	
PPX1_Sc	[41] DIKGFSVSDILKDYKQFNQ [ 97]	MFKQLNVEATRKKQVVPYLEE	730369	
PRUNE_Dm	[37] DISKLTLEVLKDKMKVLQTD [ 97]	LRQHNQVQATRKH-ILPIVKR	1079081	
h-prune.1_Hs	[34] DVSGLTTEQMLRKDKQKTIYRQ [ 94]	YLQGNTQVSRKK-LLPLLQE	11245938	

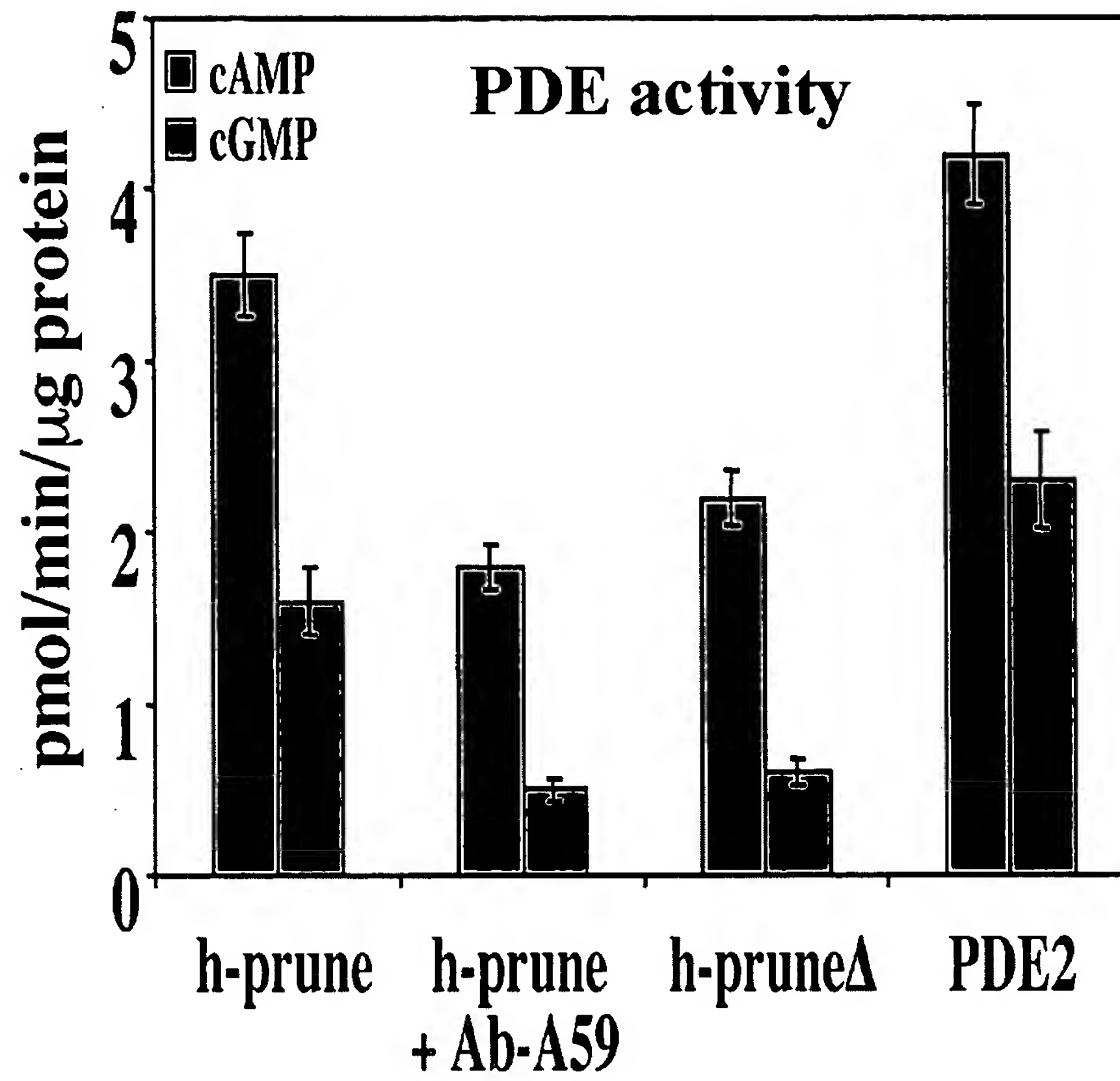
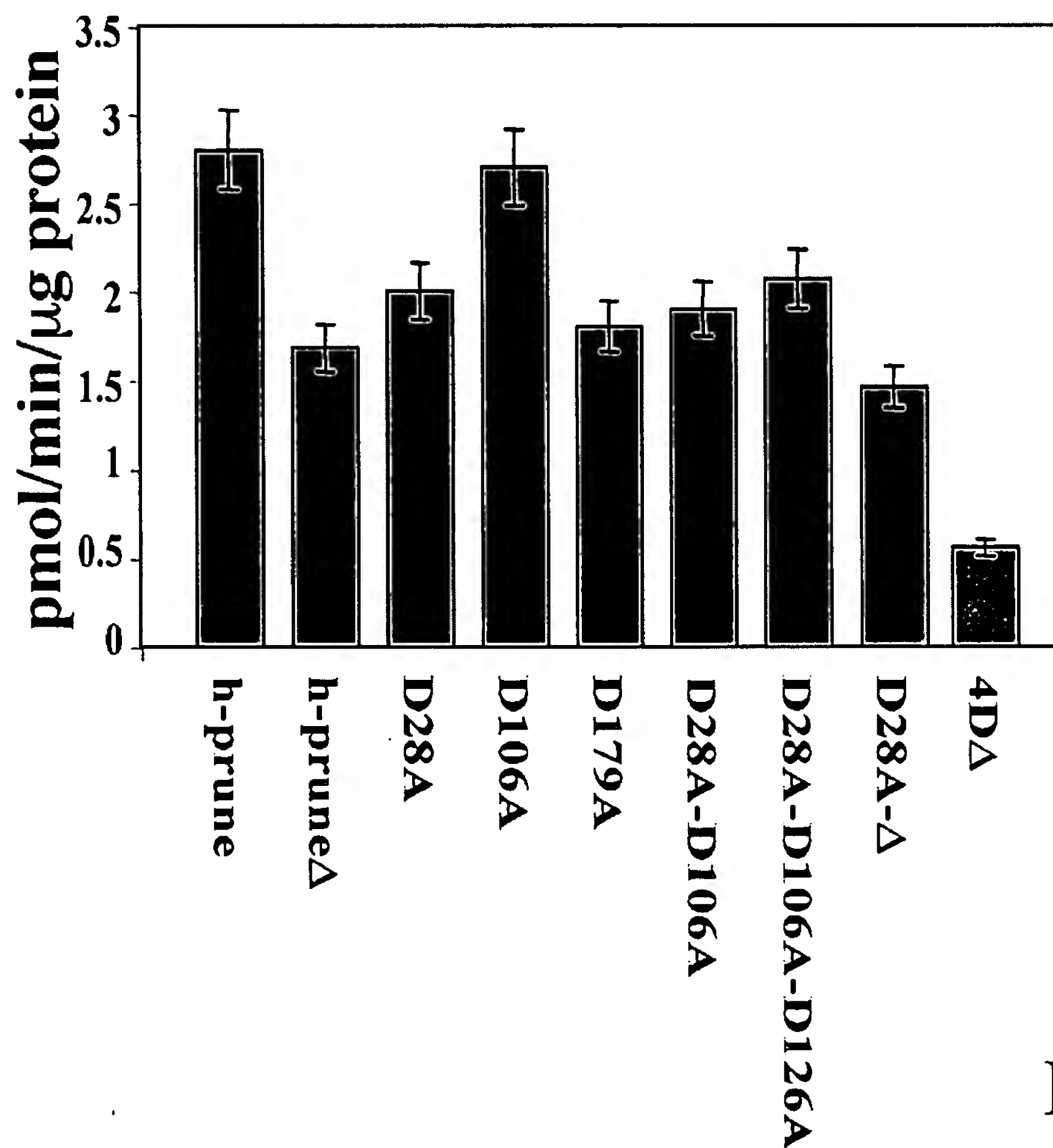
Family 2

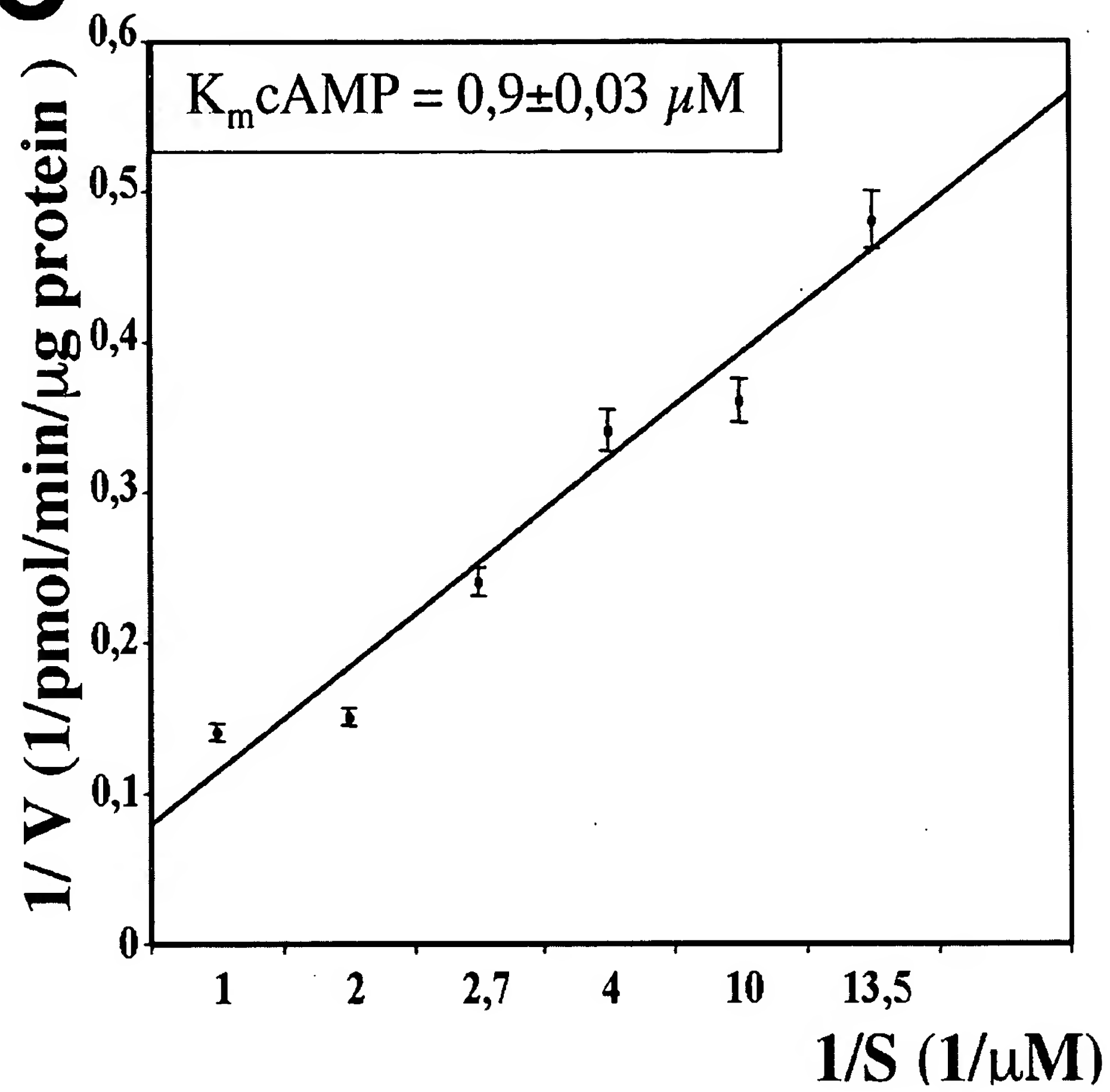
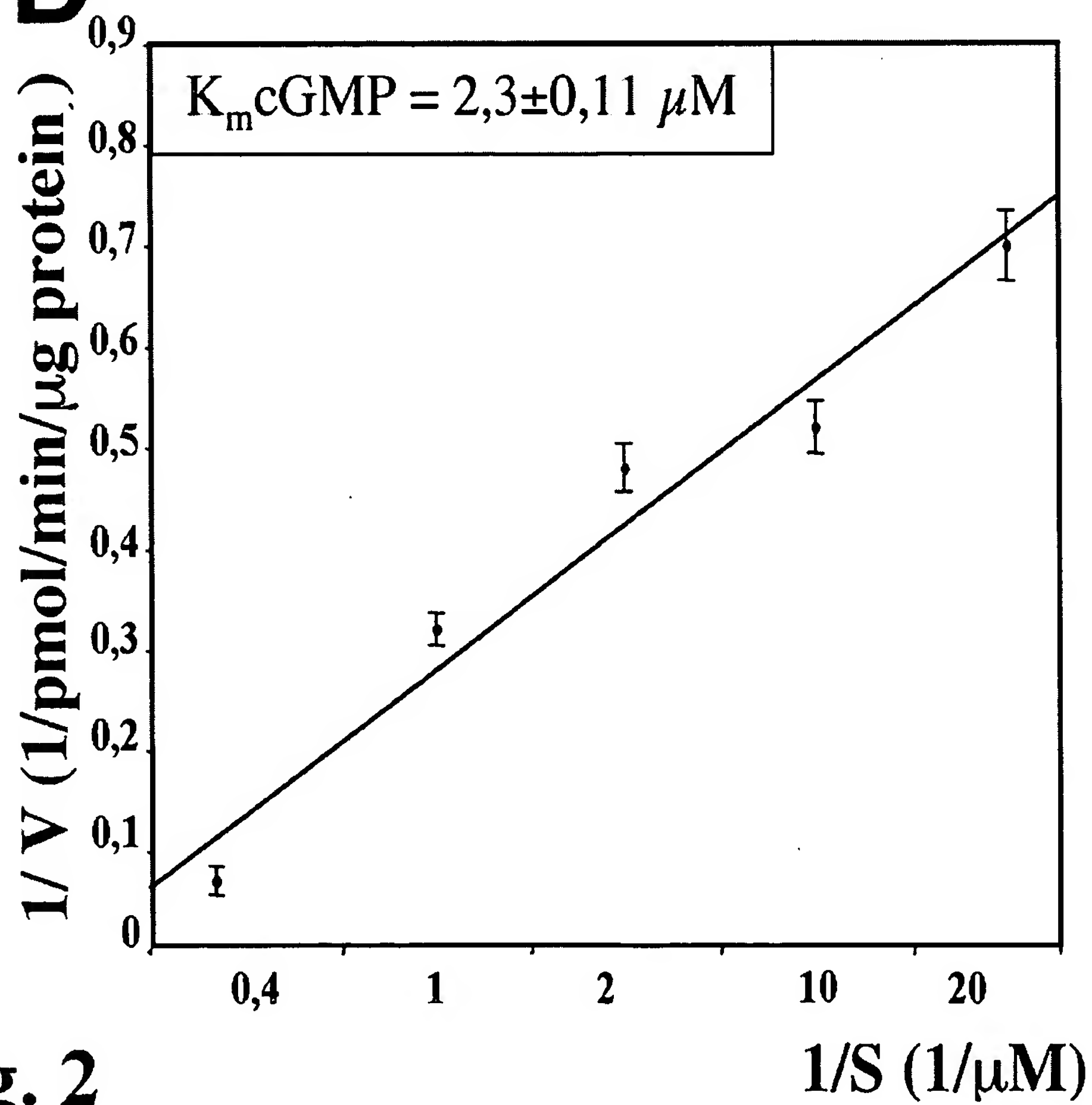
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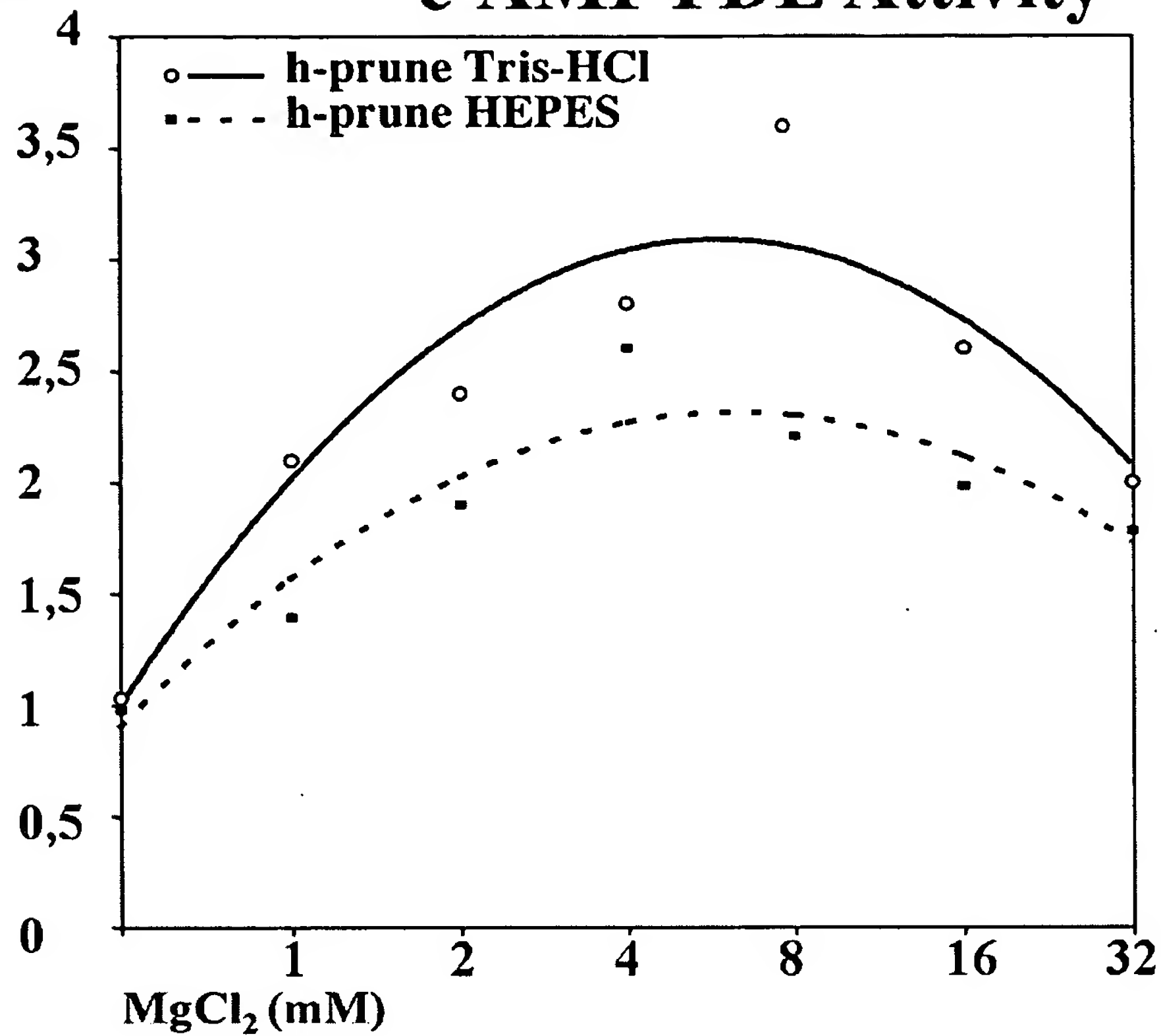
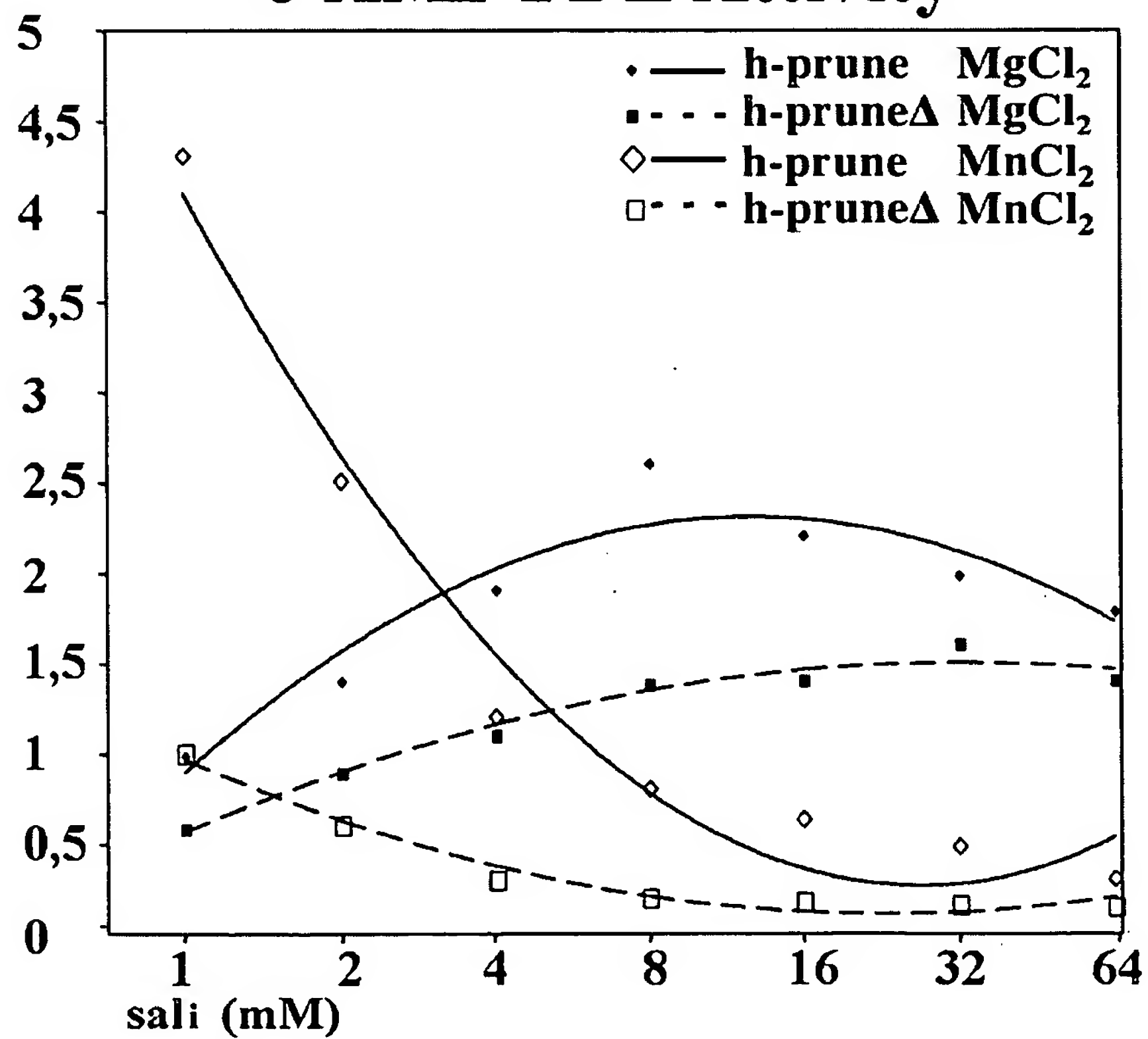
Fig. 1



**Fig. 1**

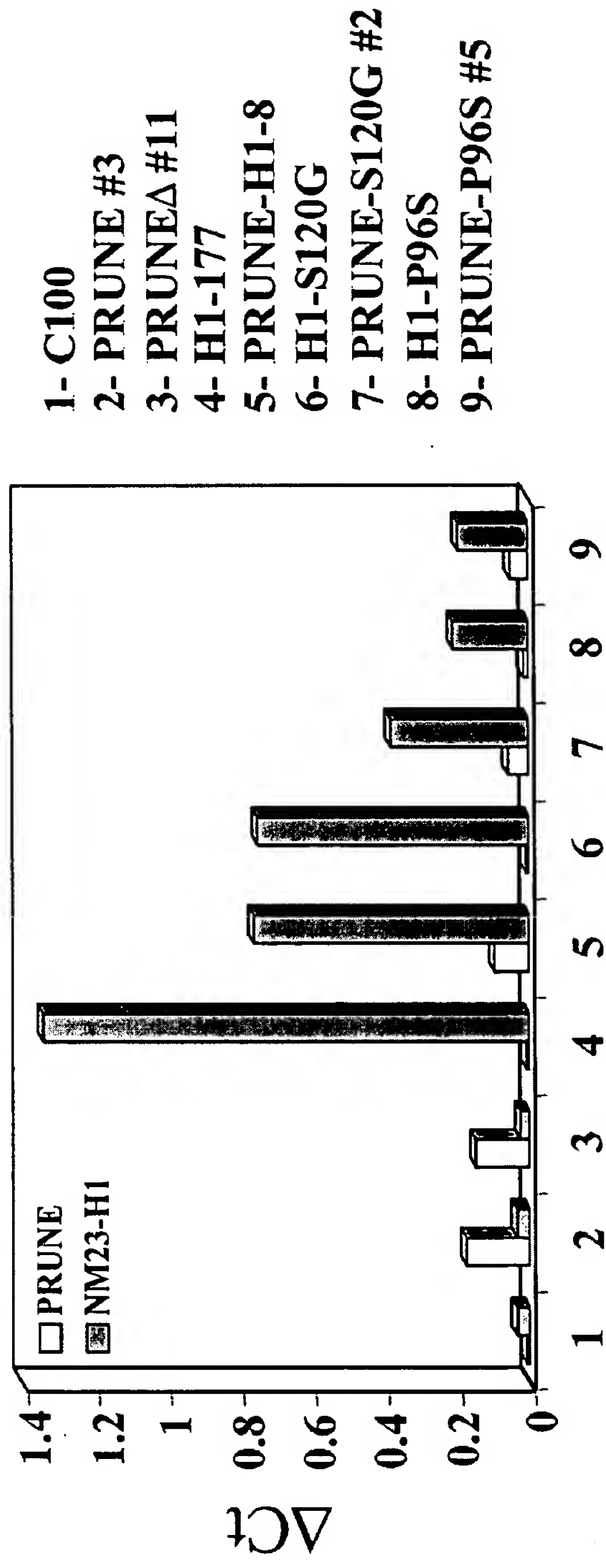
**A****B****Fig. 2**

**C****D****Fig. 2**

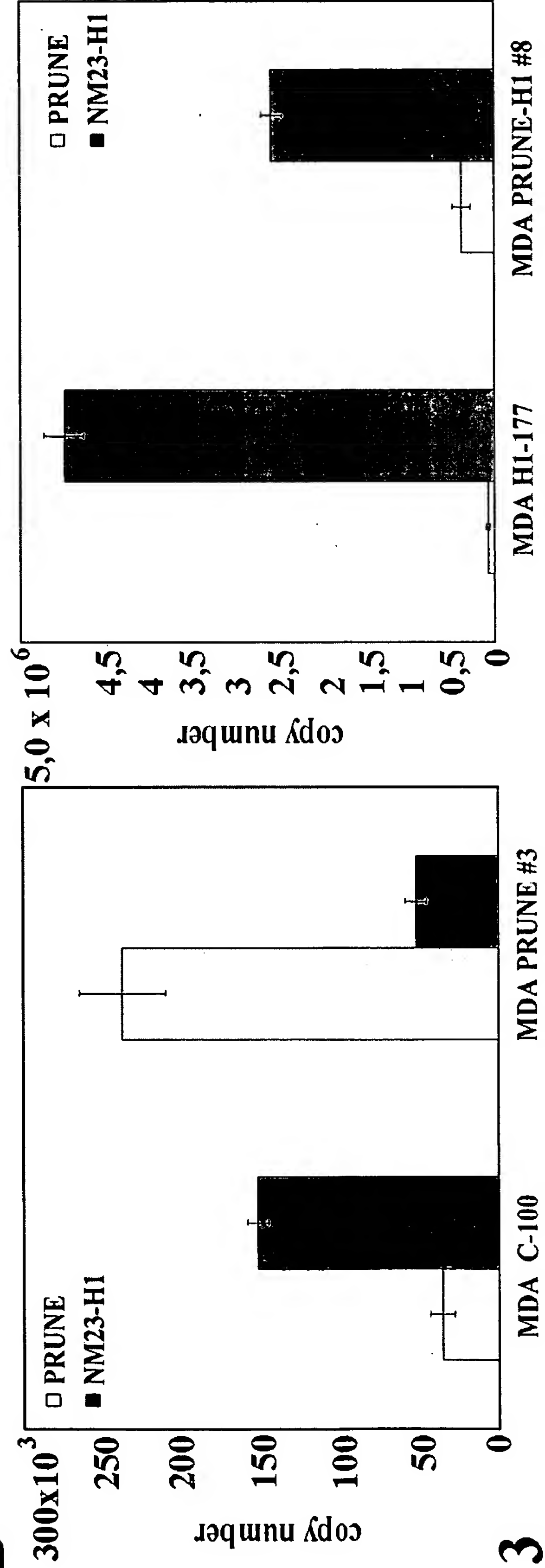
**E****c-AMP PDE Activity****F****c-AMP PDE Activity****Fig. 2**



**A**

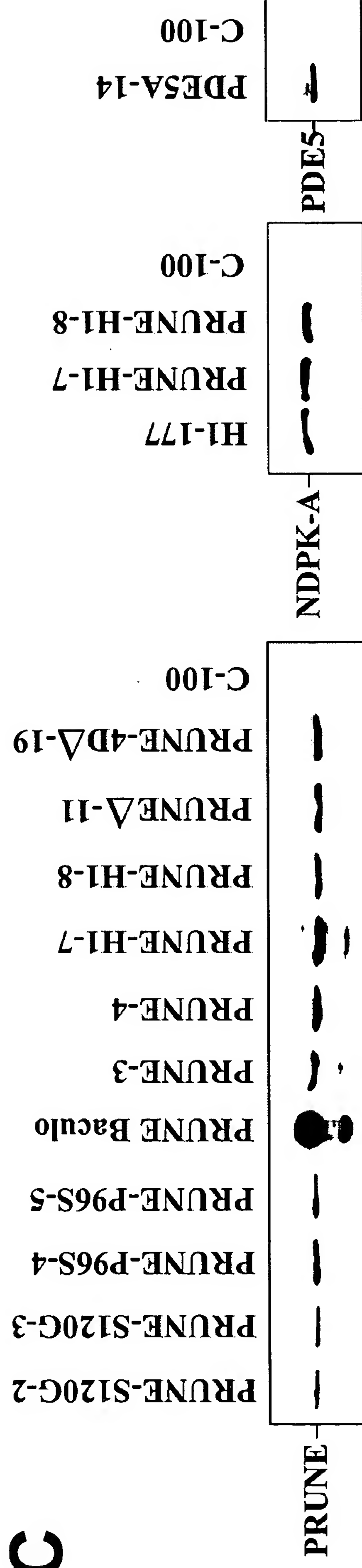


**B**



**Fig. 3**

C



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D

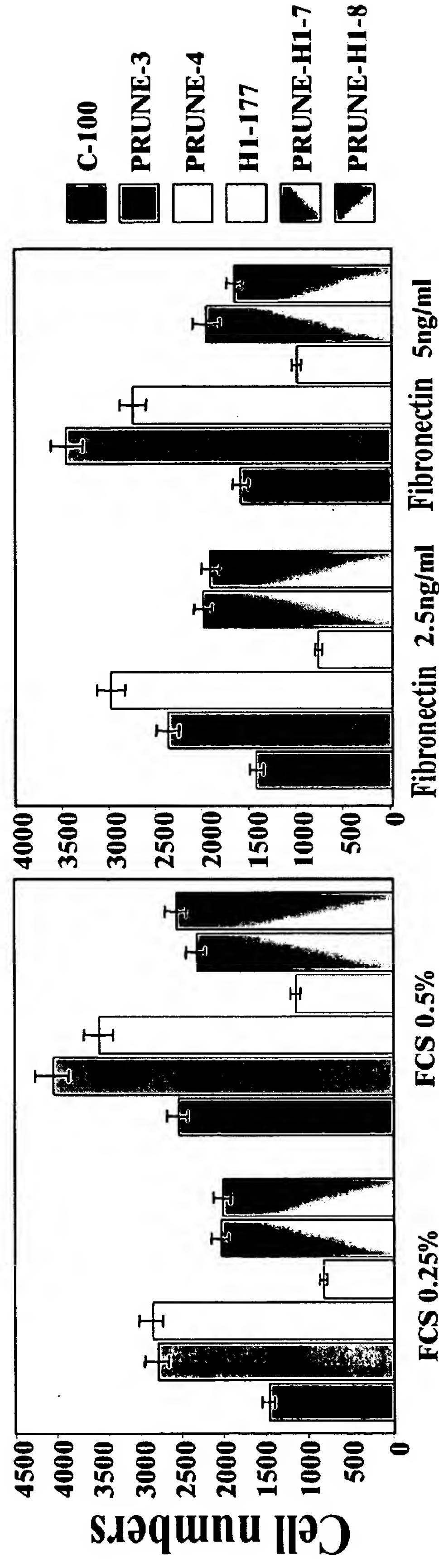
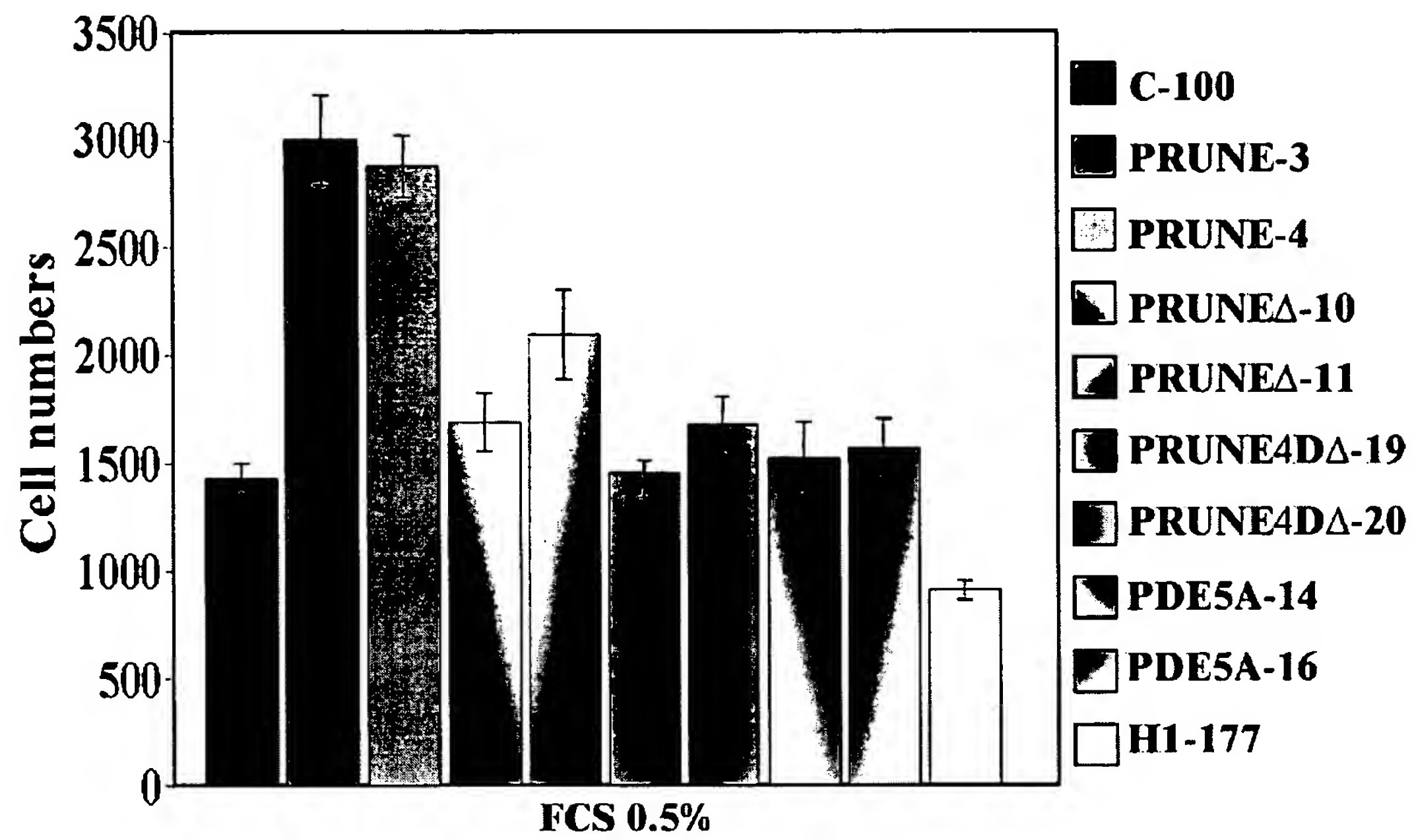
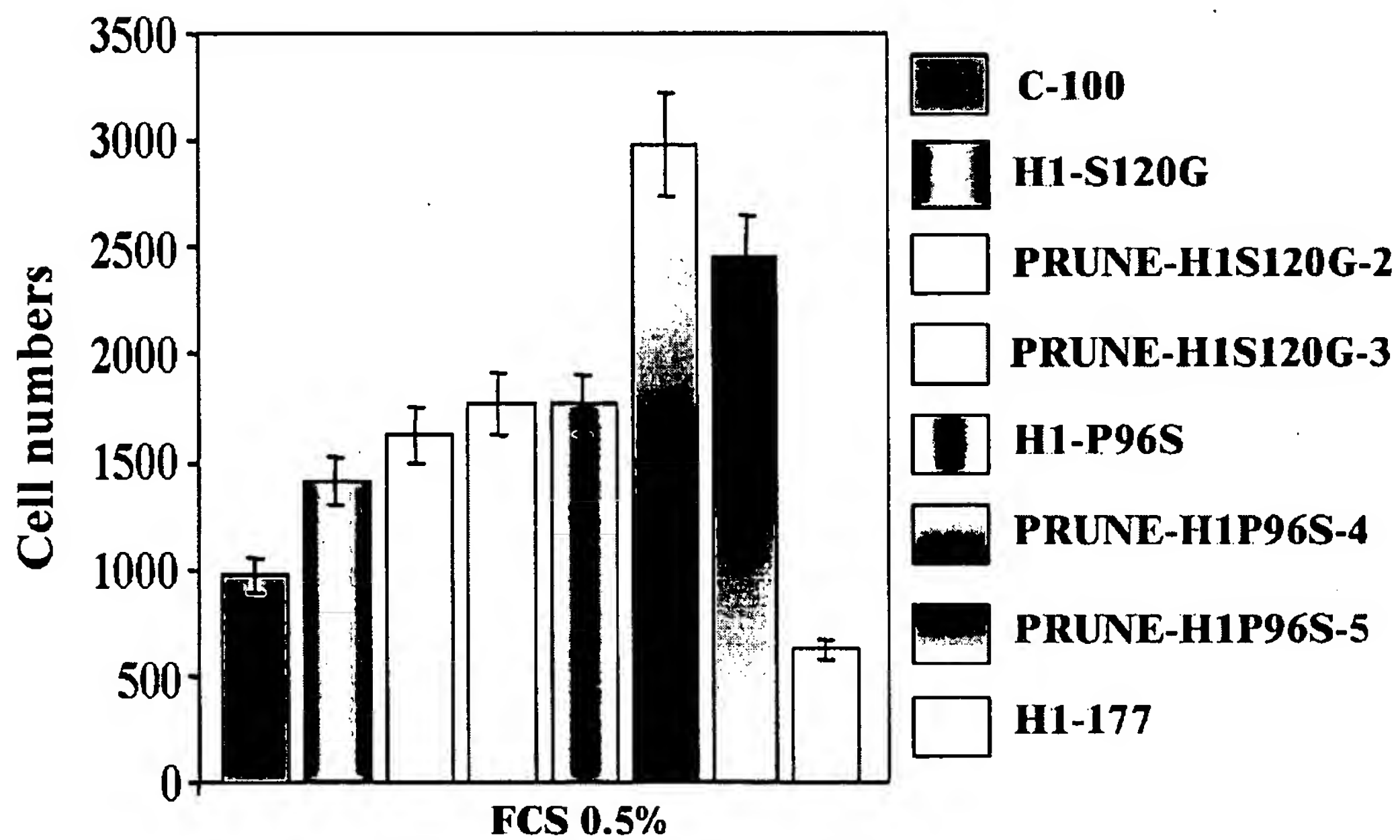
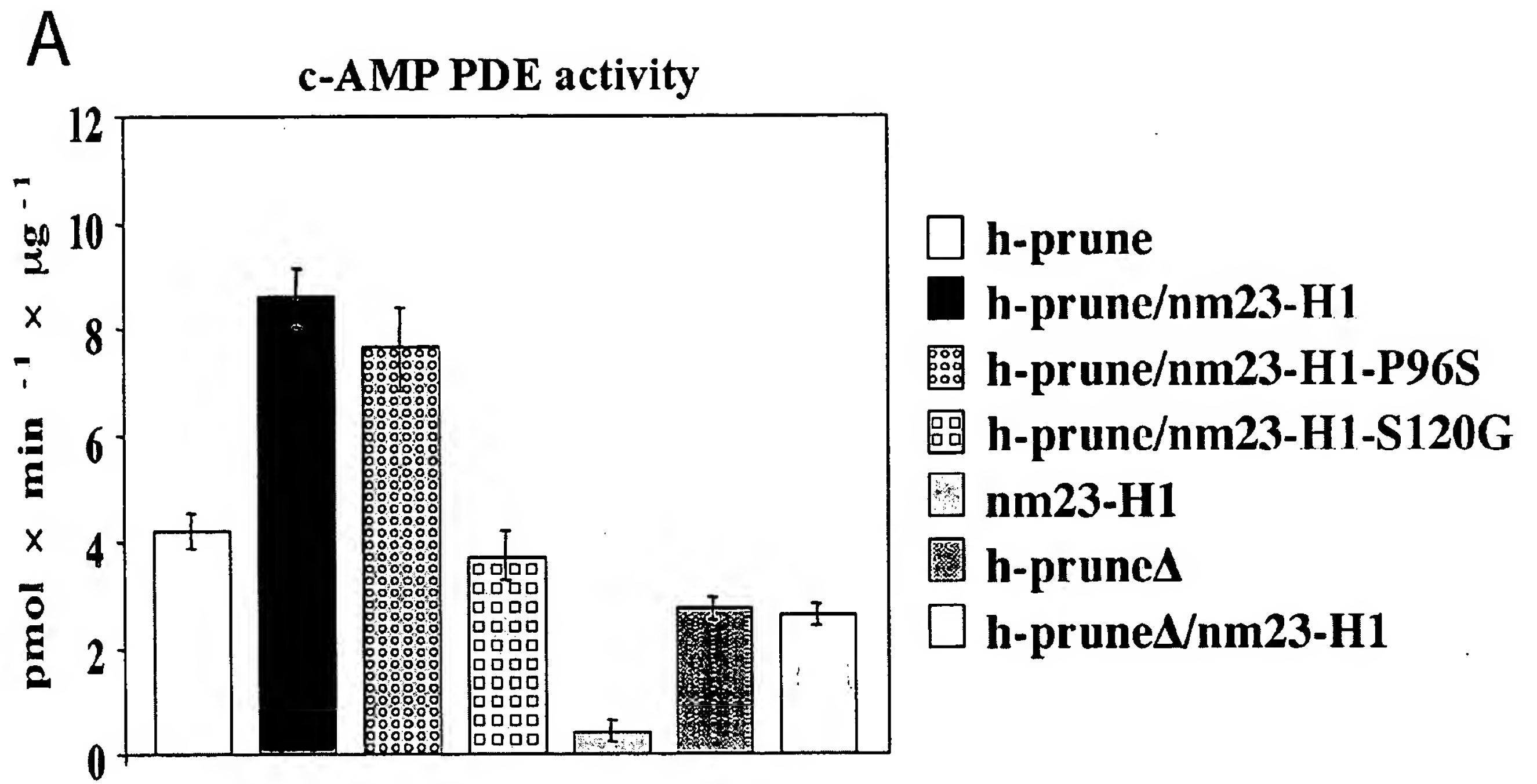


Fig. 3

**E****F****Fig. 3**





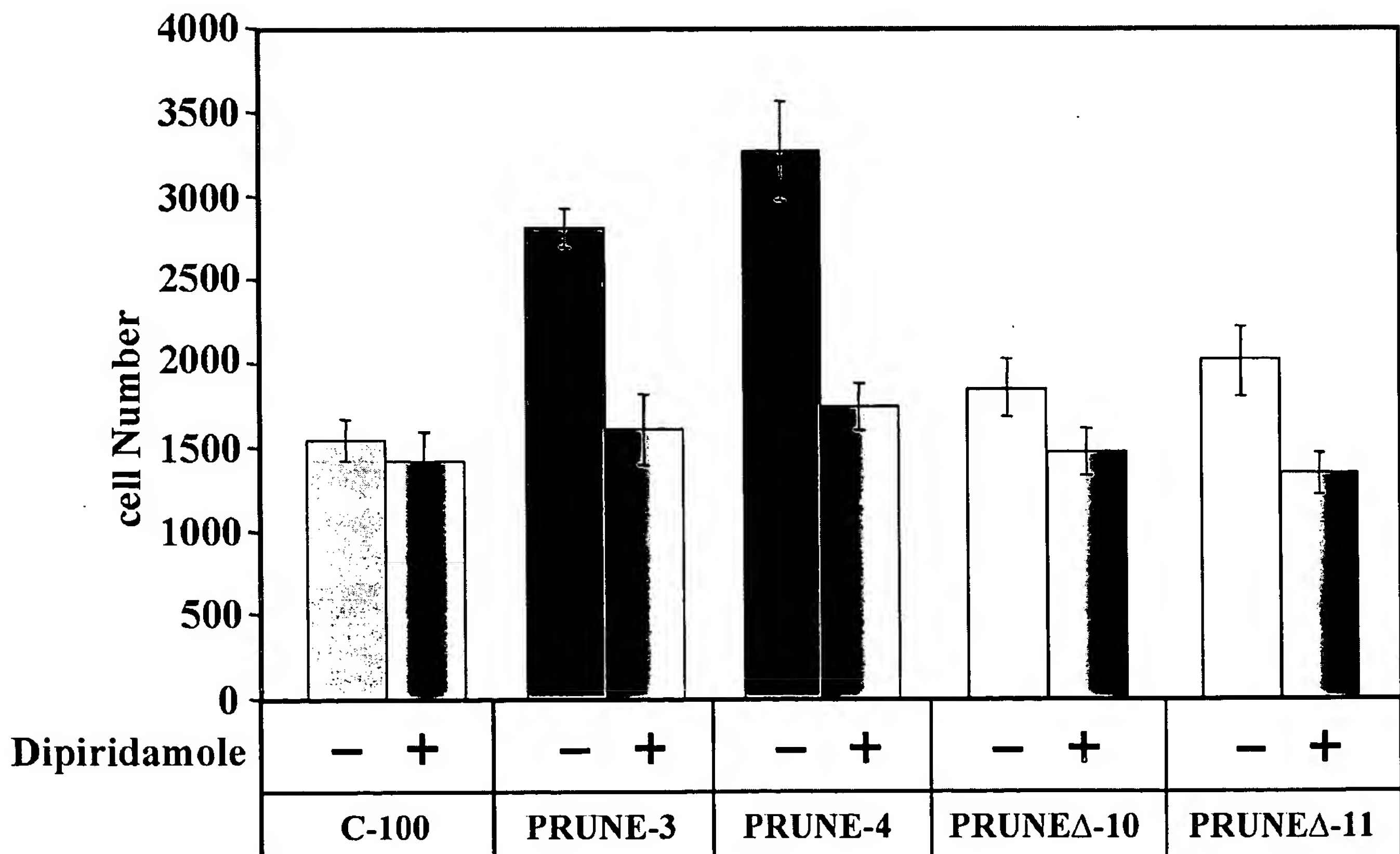
**B**

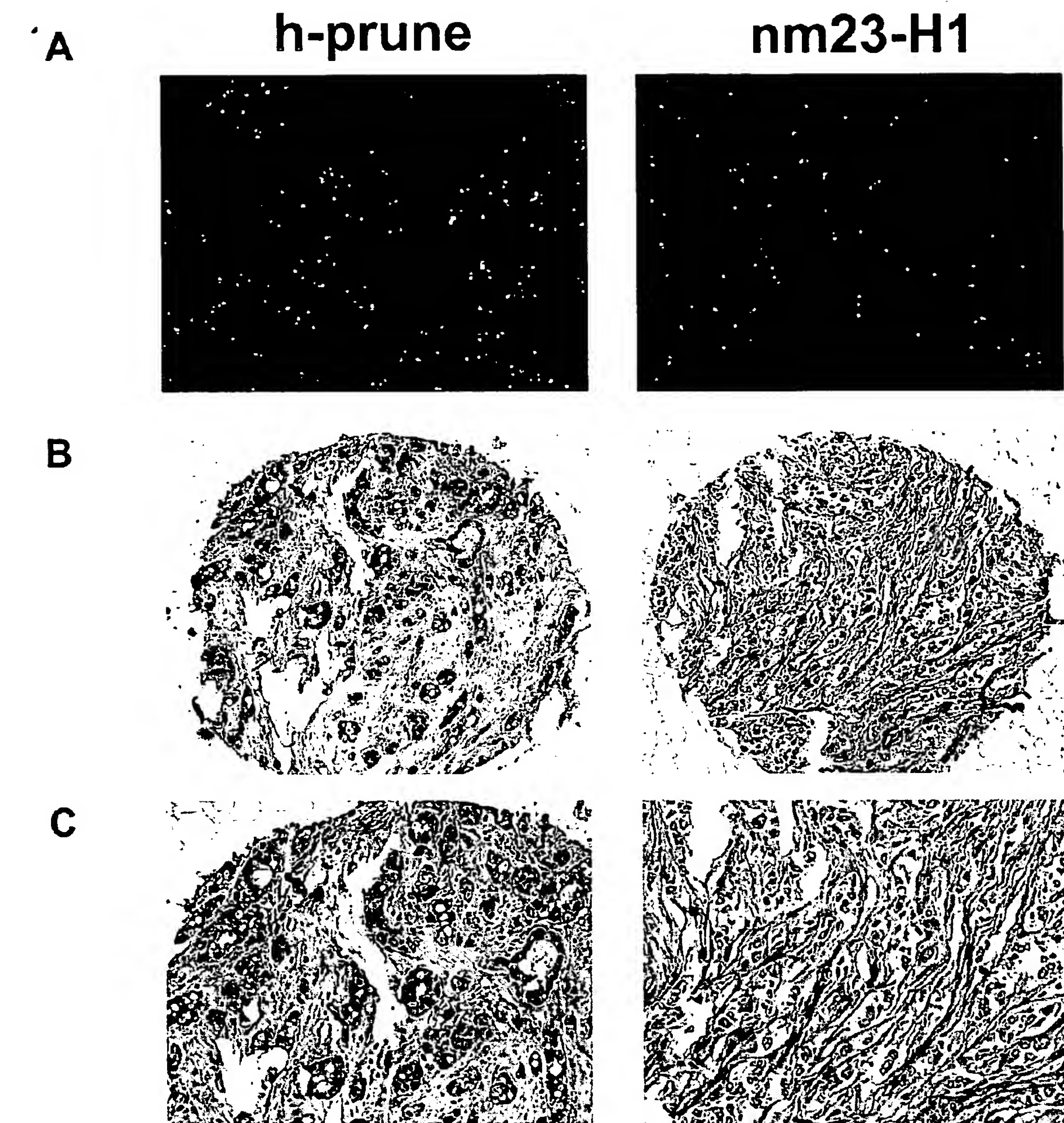
clone name	PDE h-prune Activity (pmol $\times$ min <sup>-1</sup> $\times$ $\mu$ g <sup>-1</sup> )	Mobility cell number
MDA C-100	3.8 $\pm$ 0.7	1548 $\pm$ 84
MDA H1-177	2.2 $\pm$ 0.4	928 $\pm$ 73
MDA PRUNE #3	35 $\pm$ 5.3	2812 $\pm$ 294
MDA PRUNE #4	28.7 $\pm$ 2.5	3272 $\pm$ 271
MDA PRUNE $\Delta$ #10	16.8 $\pm$ 1.2	1682 $\pm$ 64
MDA PRUNE $\Delta$ #11	14.6 $\pm$ 0.9	2087 $\pm$ 97
MDA PRUNE-H1 #7	18.8 $\pm$ 2.6	2048 $\pm$ 93
MDA PRUNE-H1 #8	22 $\pm$ 4.2	2006 $\pm$ 87
MDA H1S120G	2.4 $\pm$ 0.8	1328 $\pm$ 54
MDA PRUNE-H1S120G #2	4.4 $\pm$ 1.6	1624 $\pm$ 89
MDA PRUNE-H1S120G #3	5.3 $\pm$ 1.4	1767 $\pm$ 108
MDA H1P96S	3.0 $\pm$ 0.3	1742 $\pm$ 38
MDA PRUNE-H1P96S #4	19.2 $\pm$ 0.3	2982 $\pm$ 184
MDA PRUNE-H1P96S #5	11.6 $\pm$ 0.4	2448 $\pm$ 143

**Fig. 4**

**A**

Inibitor	Selective for a PDE type	IC <sub>50</sub> μM	h-prune IC <sub>50</sub> μM
Cilostamide	PDE3	0.05	>100
Dipiridamole	PDE5/6/9/10/11	0.9/0.38/4.5/1.1/0.37	0.78±0.05
IBMX	not selective	2-59	40.2±0.8
Milrinone	PDE3	1.3	>100
Rolipram	PDE4	2.0	>100
Vinpocetine	PDE1C	8.1	22.3±1.1
Zaprinast	PDE1/5/6	6.9/0.76/0.15	>100
Sulindac	cGMP PDEs	—	>100

**B****Fig. 5**

**D**

Immunohistochemic (IHC)	IHC Grade	Fish analysis	
		PAC h-prune (1q21.3)	
		Disomy	Trisomy or more
<b>h-prune</b>	+++ / ++	<b>7</b> (12%)	<b>22</b> (37%)
	+ / 0	<b>30</b> (51%)	
<b>nm23-h1</b>	+++ / ++		<b>1</b> (2%)
	+ / 0		<b>54</b> (98%)
<b>analyzed cases TNM<sub>I</sub></b>		<b>59</b>	<b>55</b>

**Fig. 6**

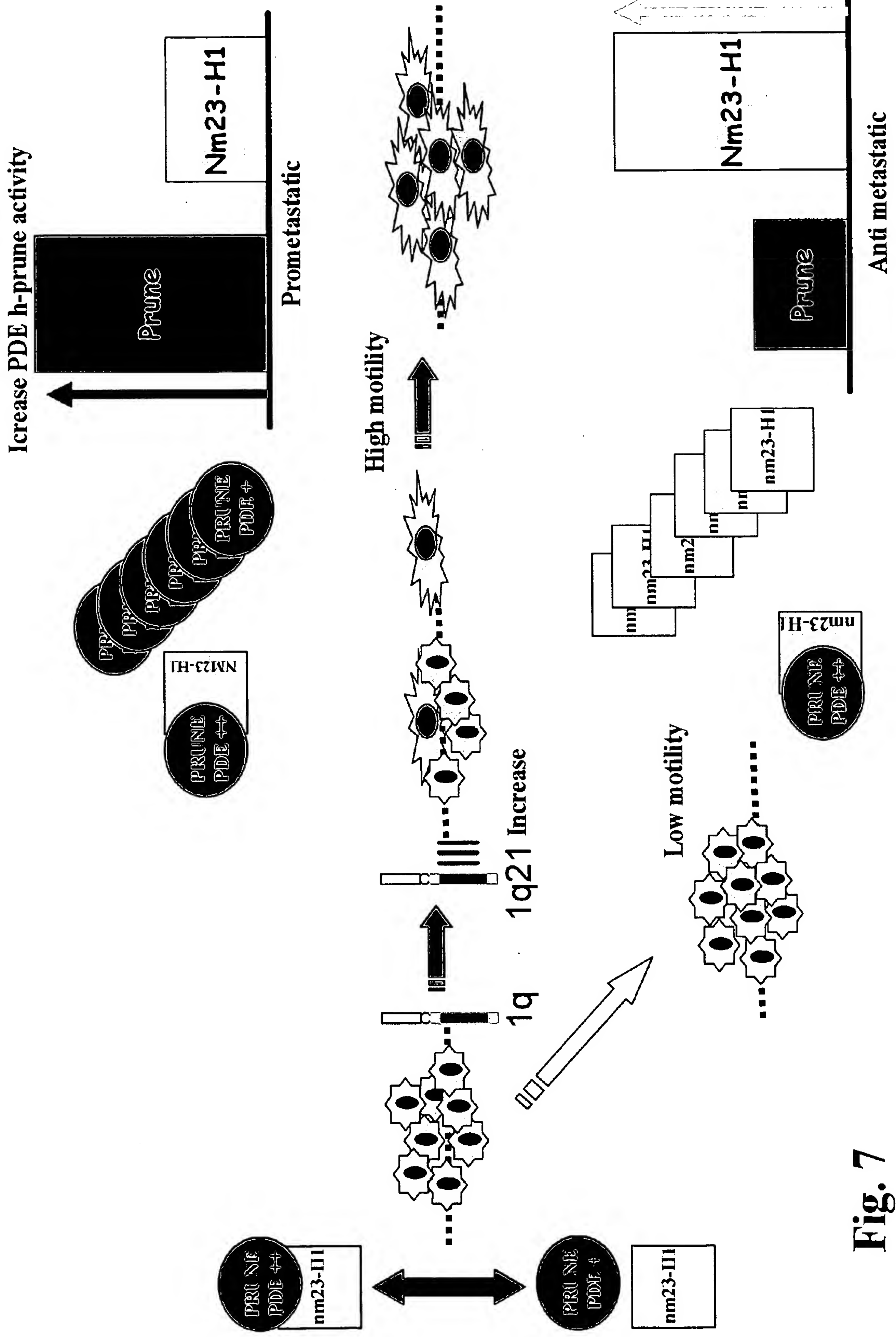
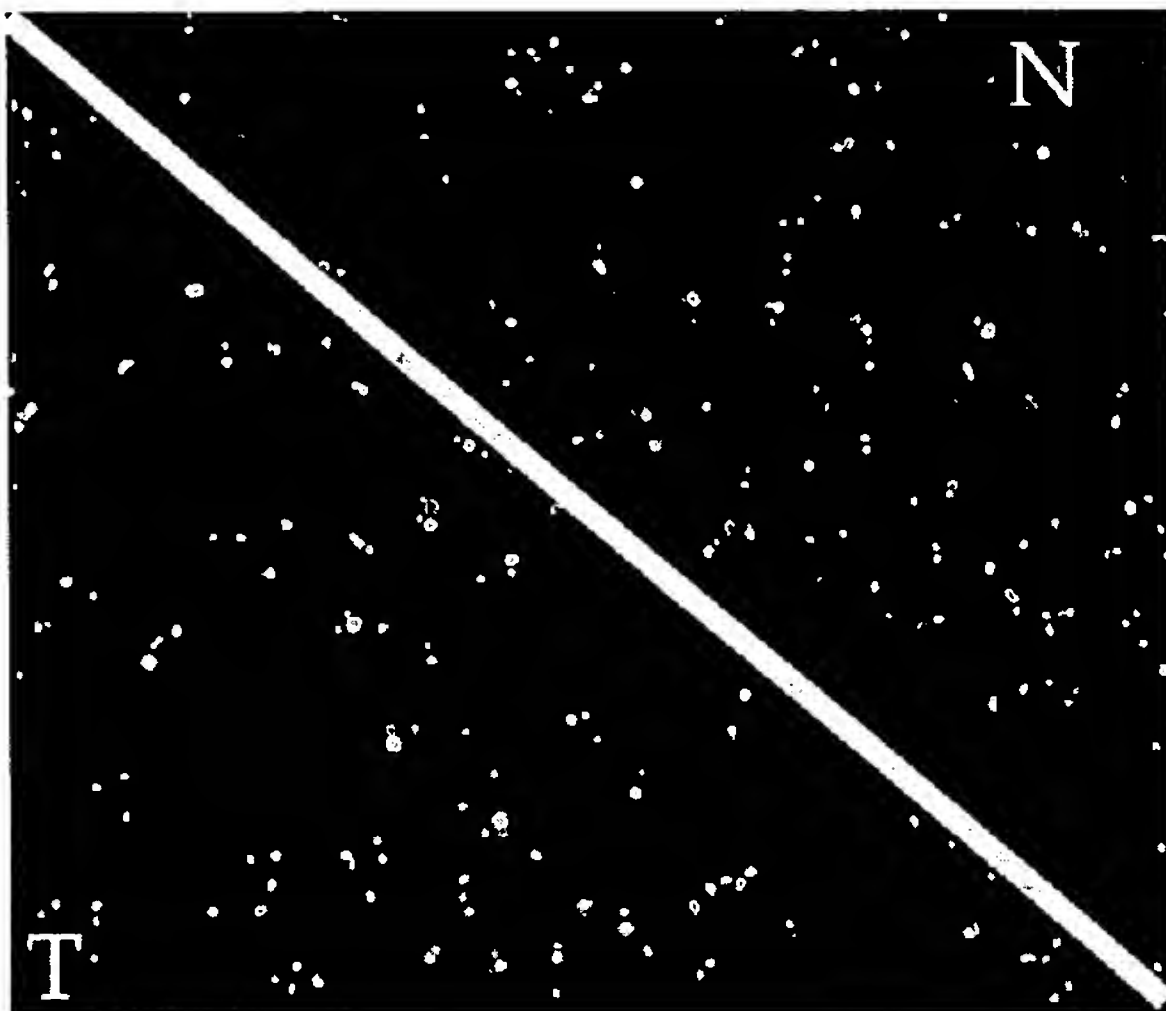


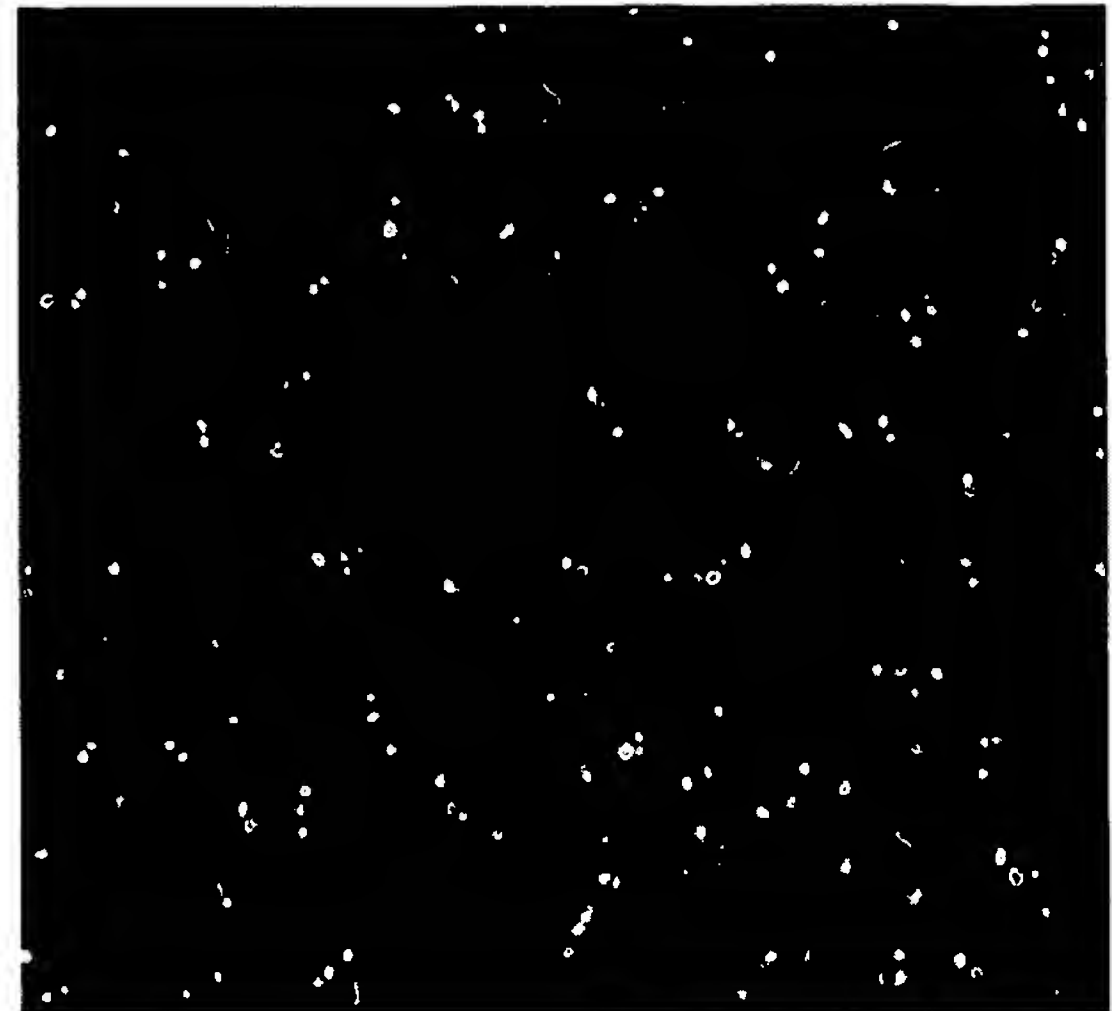
Fig. 7



**A**

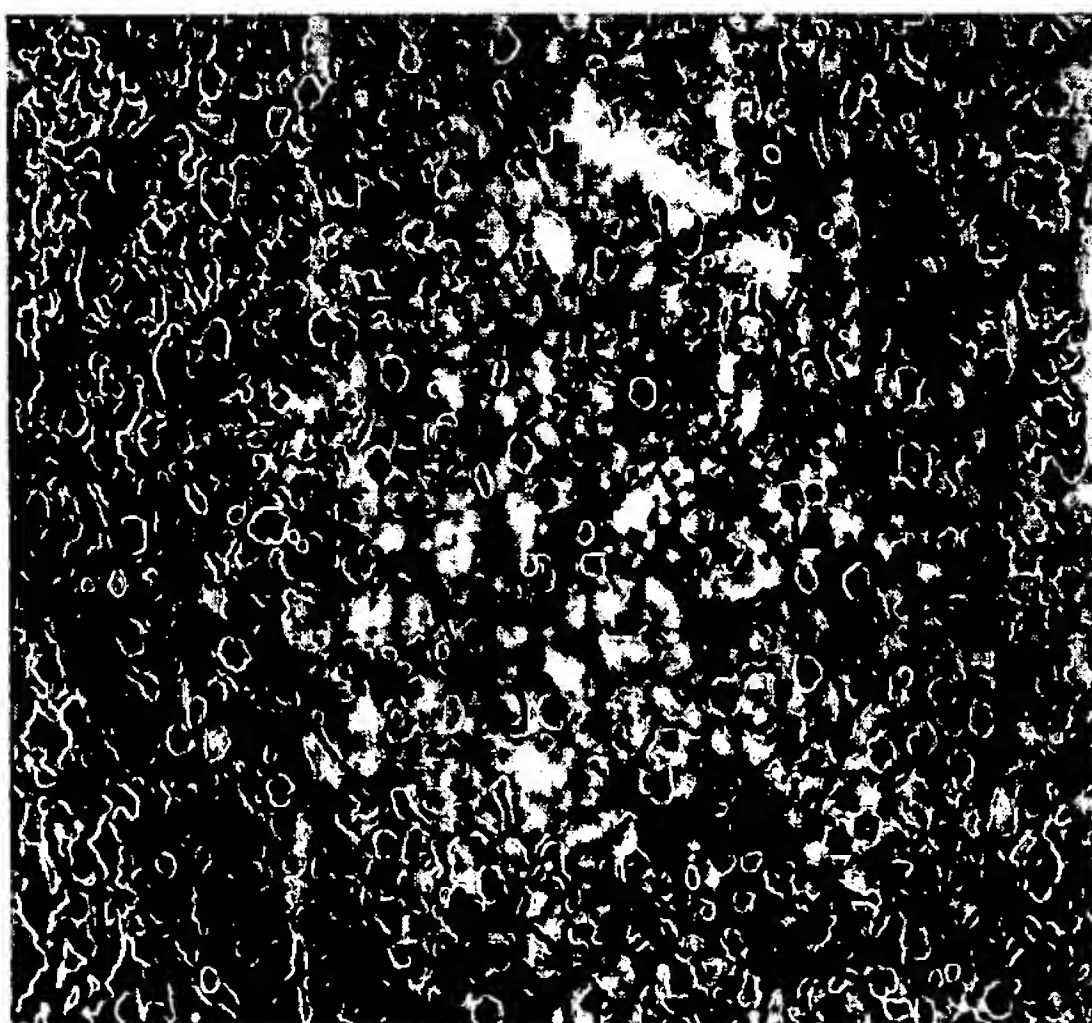


Normal and tumoral tissue

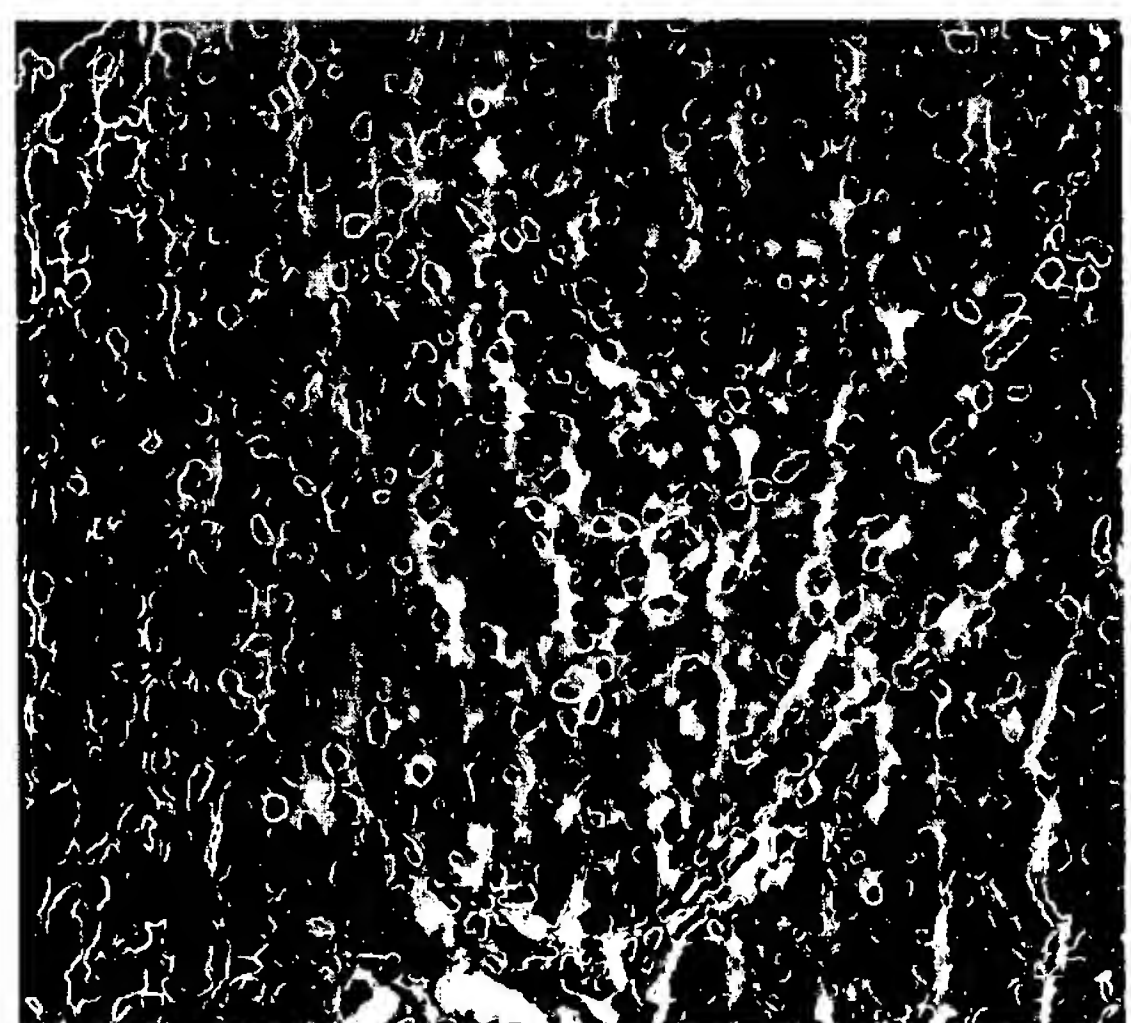


Tumoral tissue  
(not metastatic)

**B**



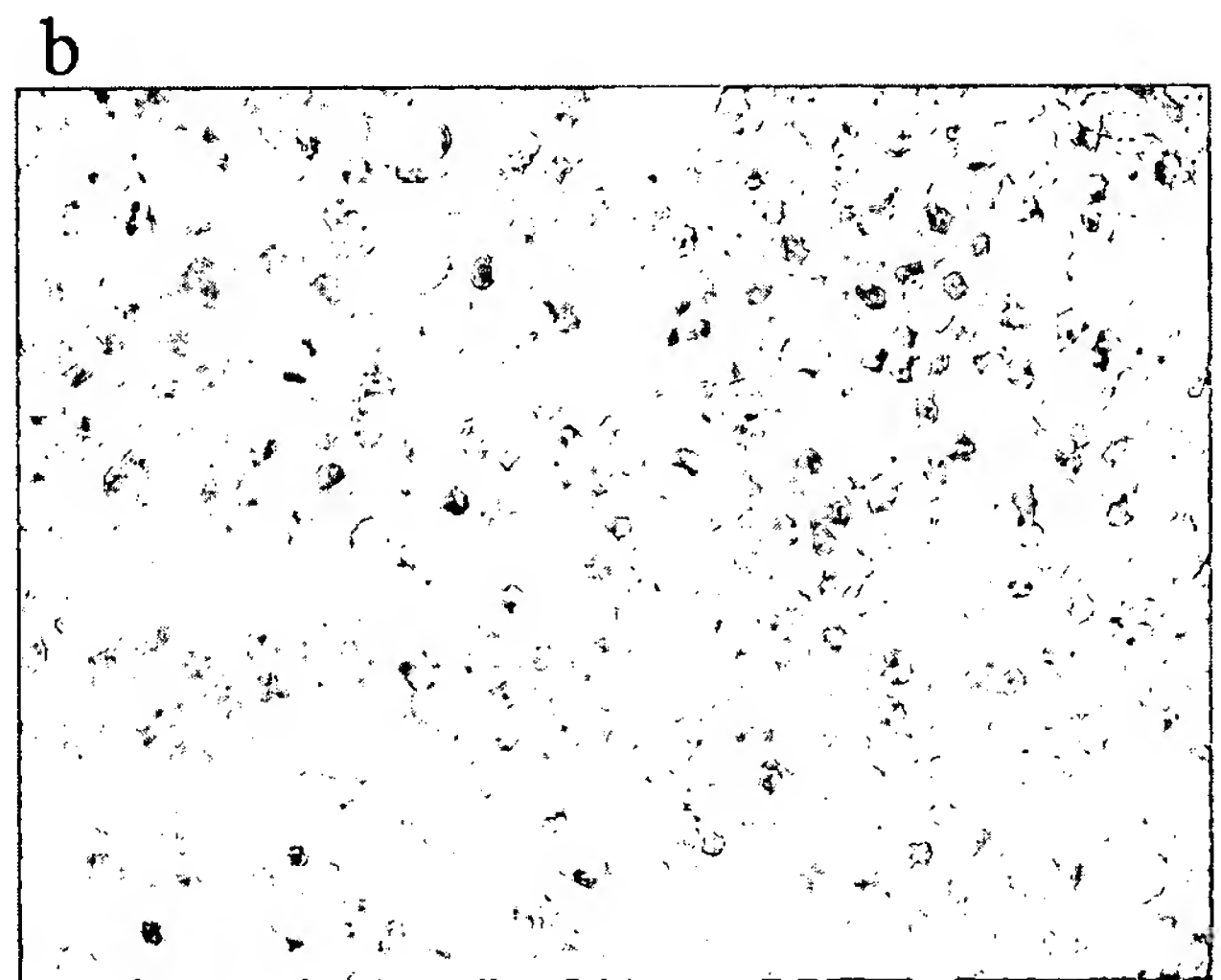
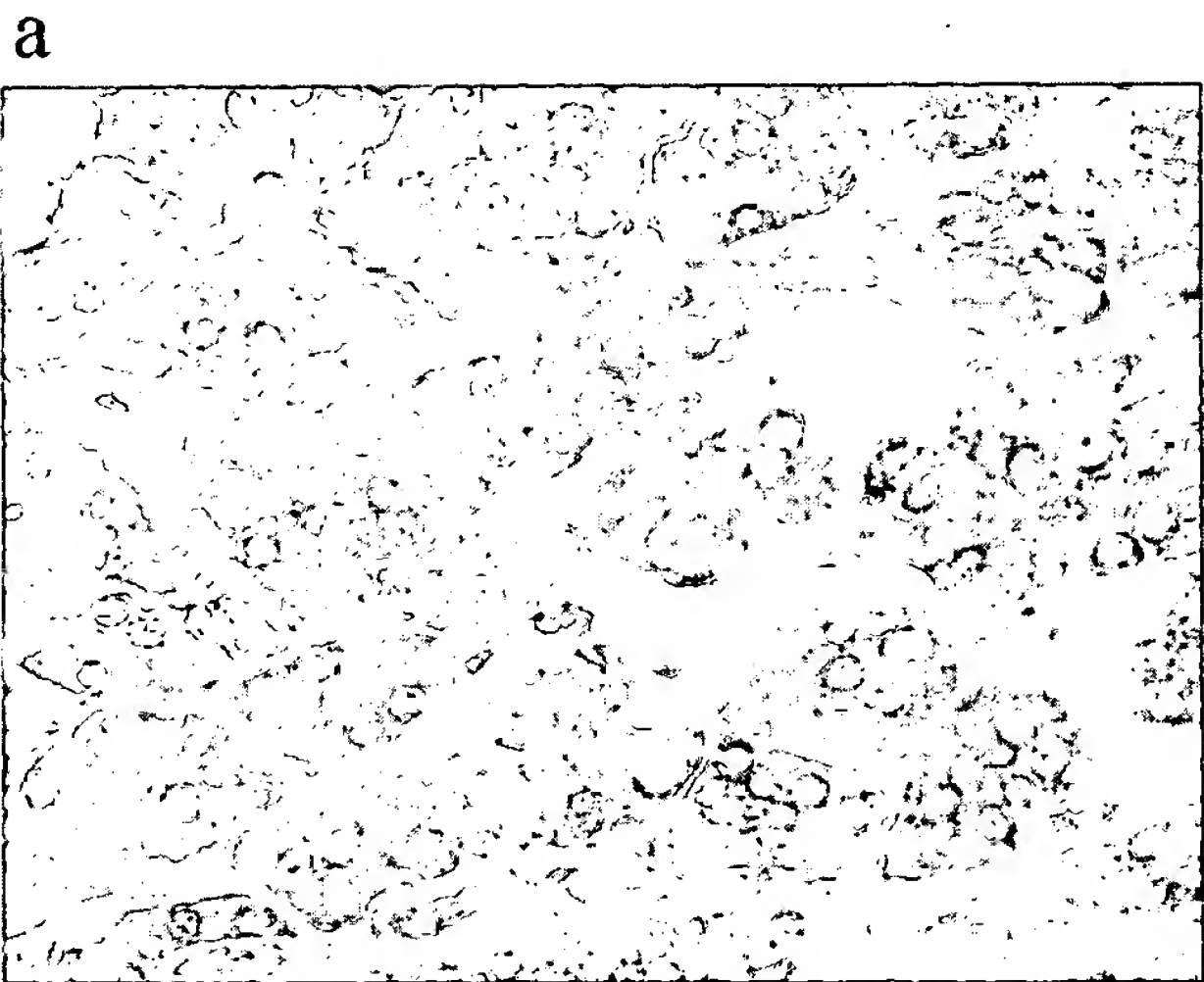
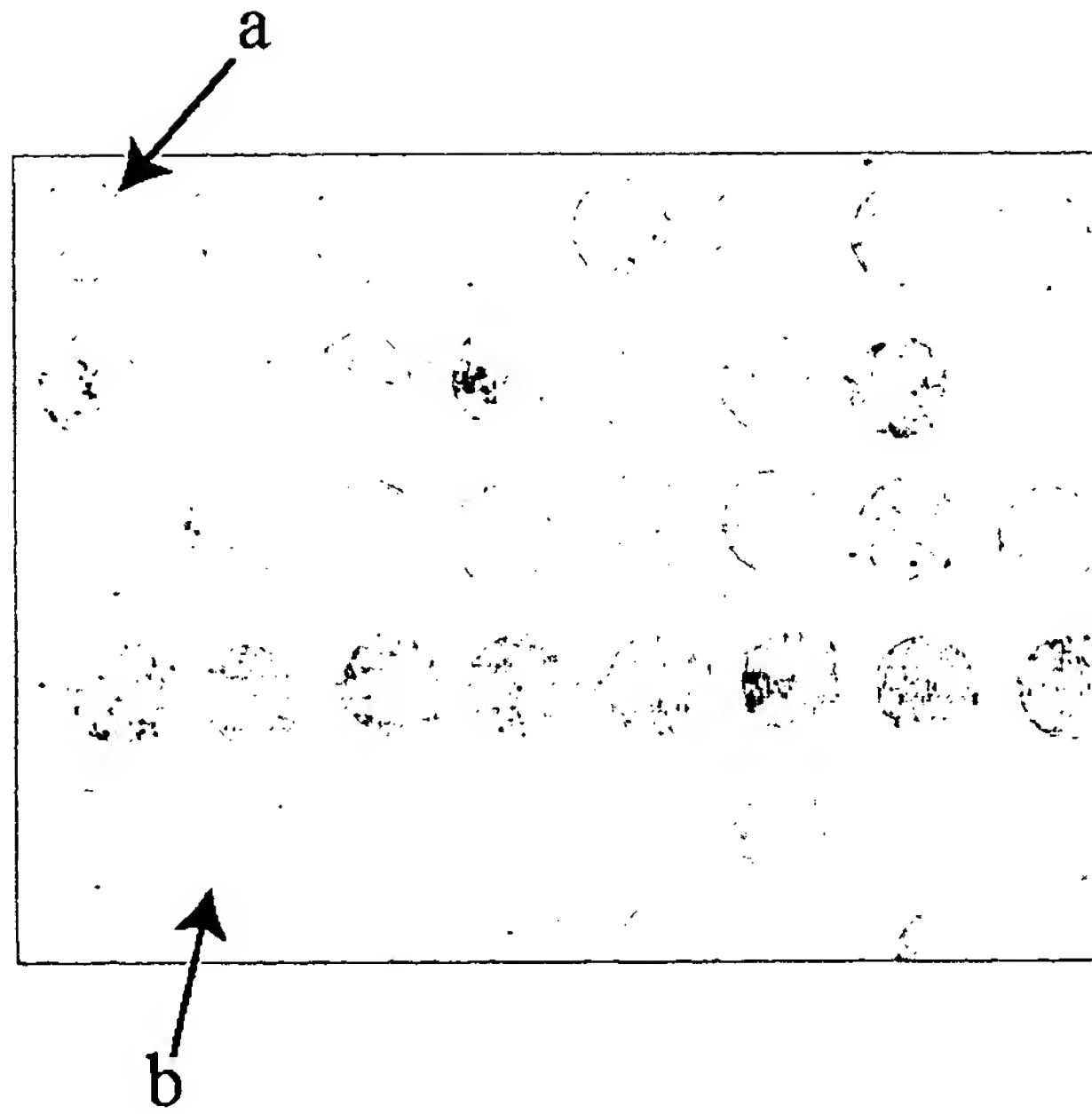
Normal tissue



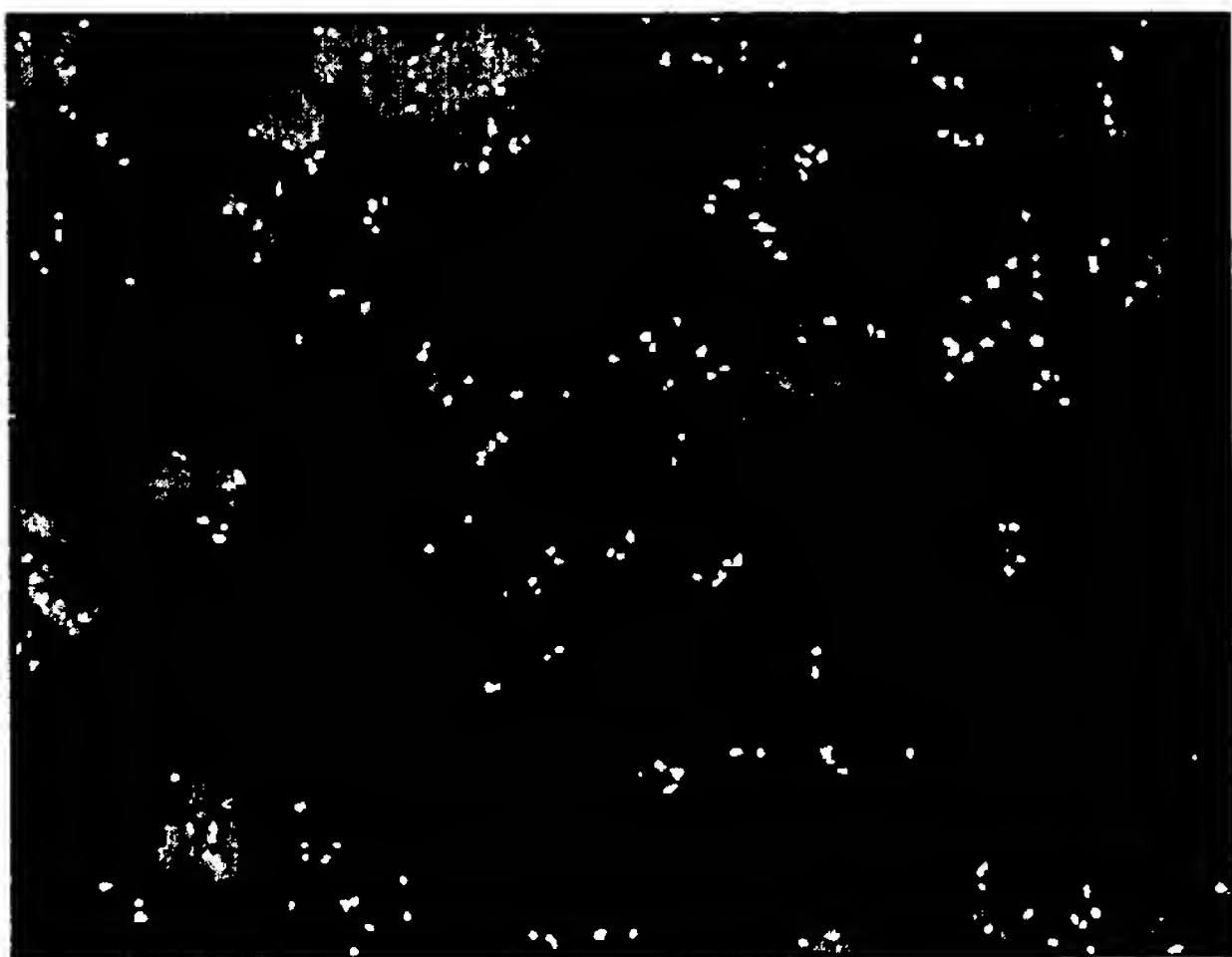
Tumoral tissue  
(not metastatic)

**Fig. 8**





A)

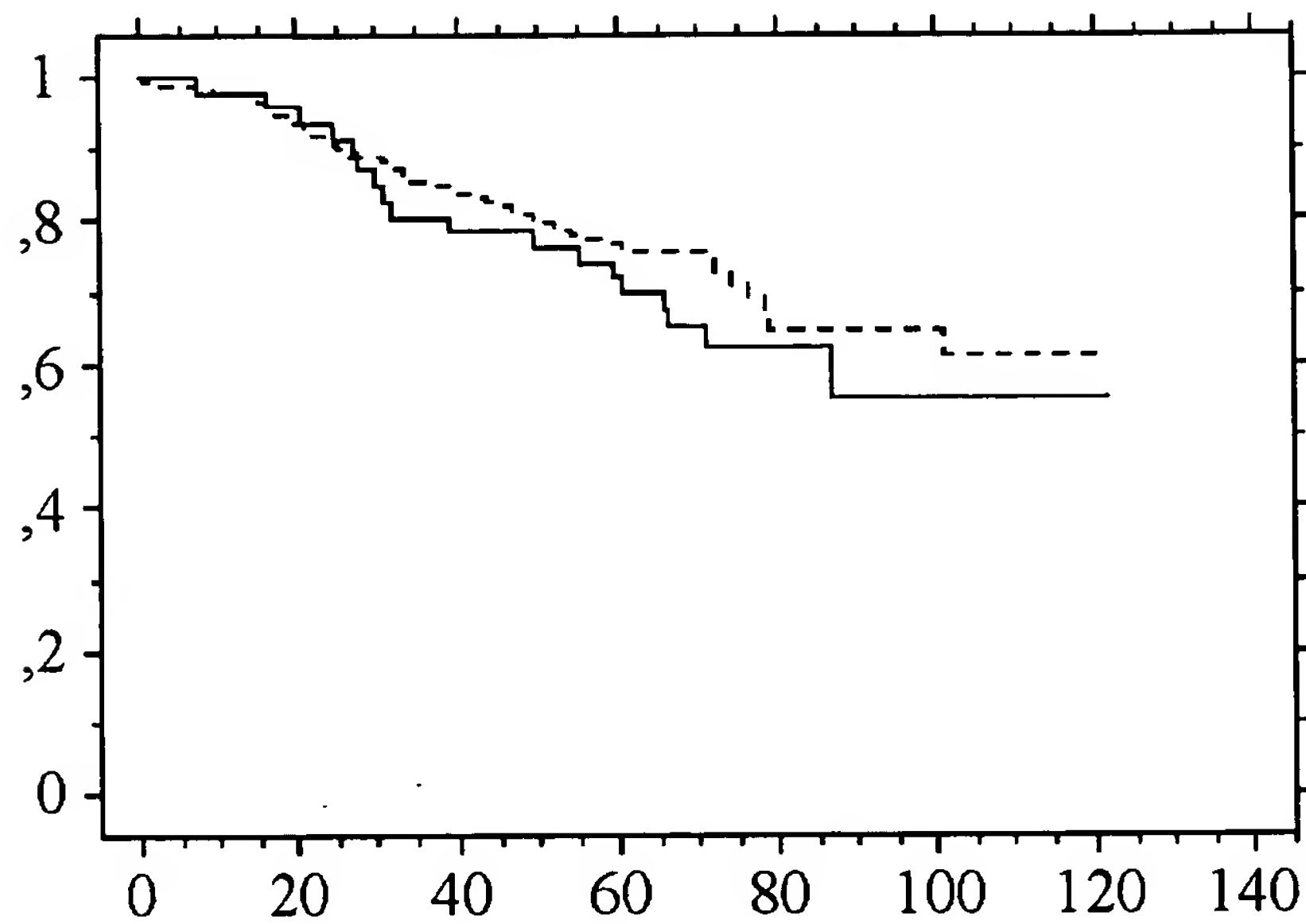


B)

**Fig. 9**

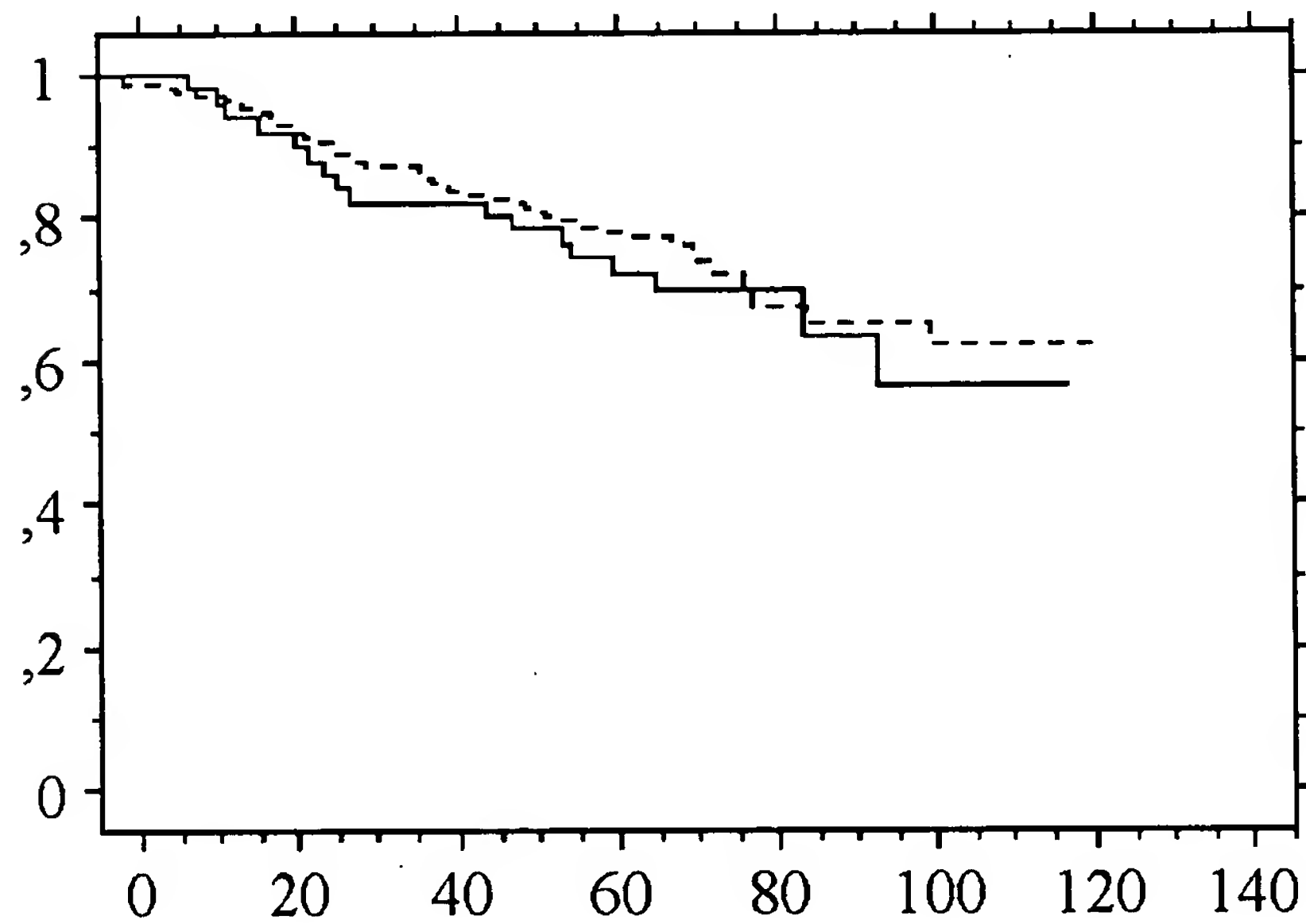
A)

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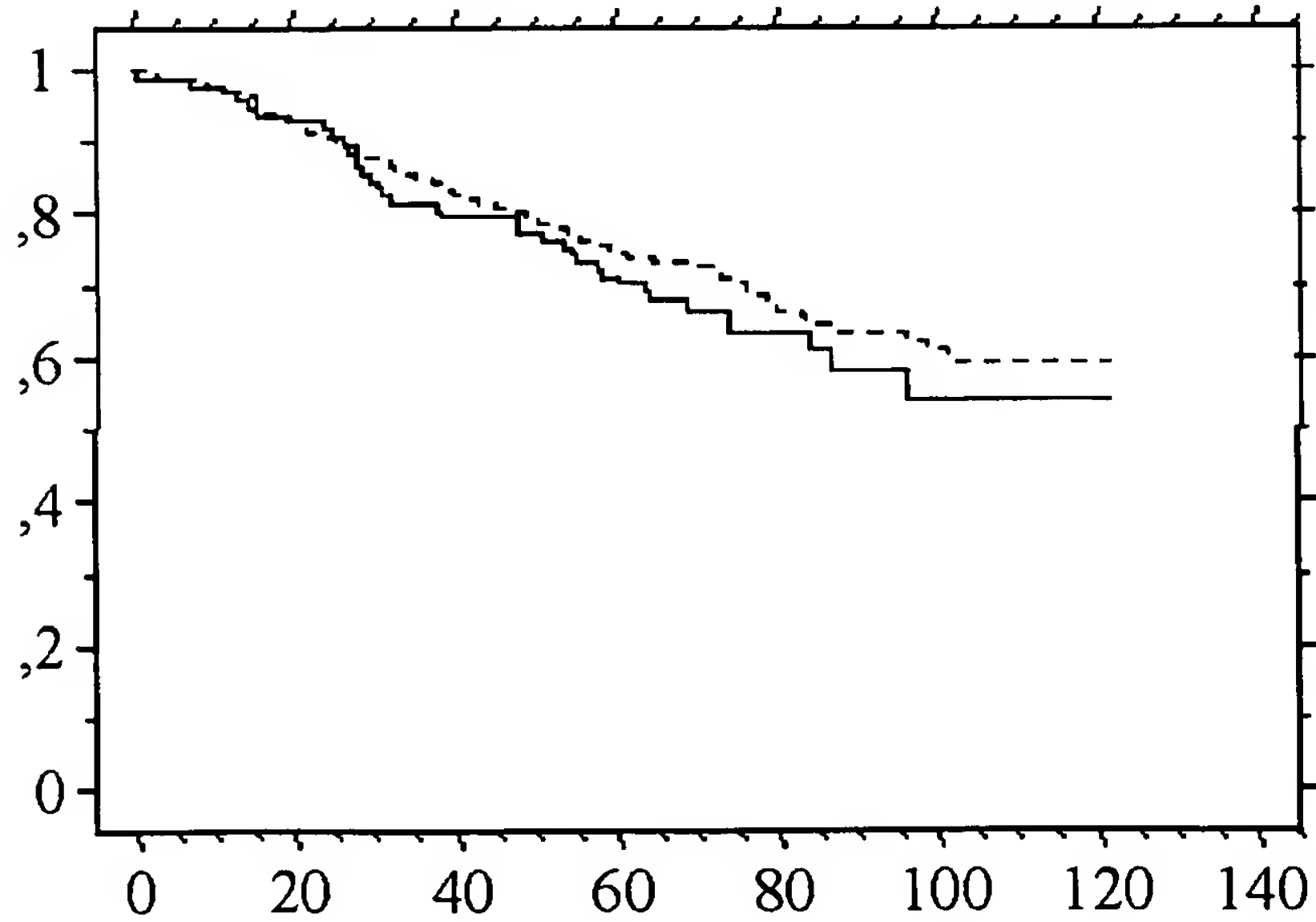
----- nm23-H1 positive  
—— nm23-H1 negative

B)



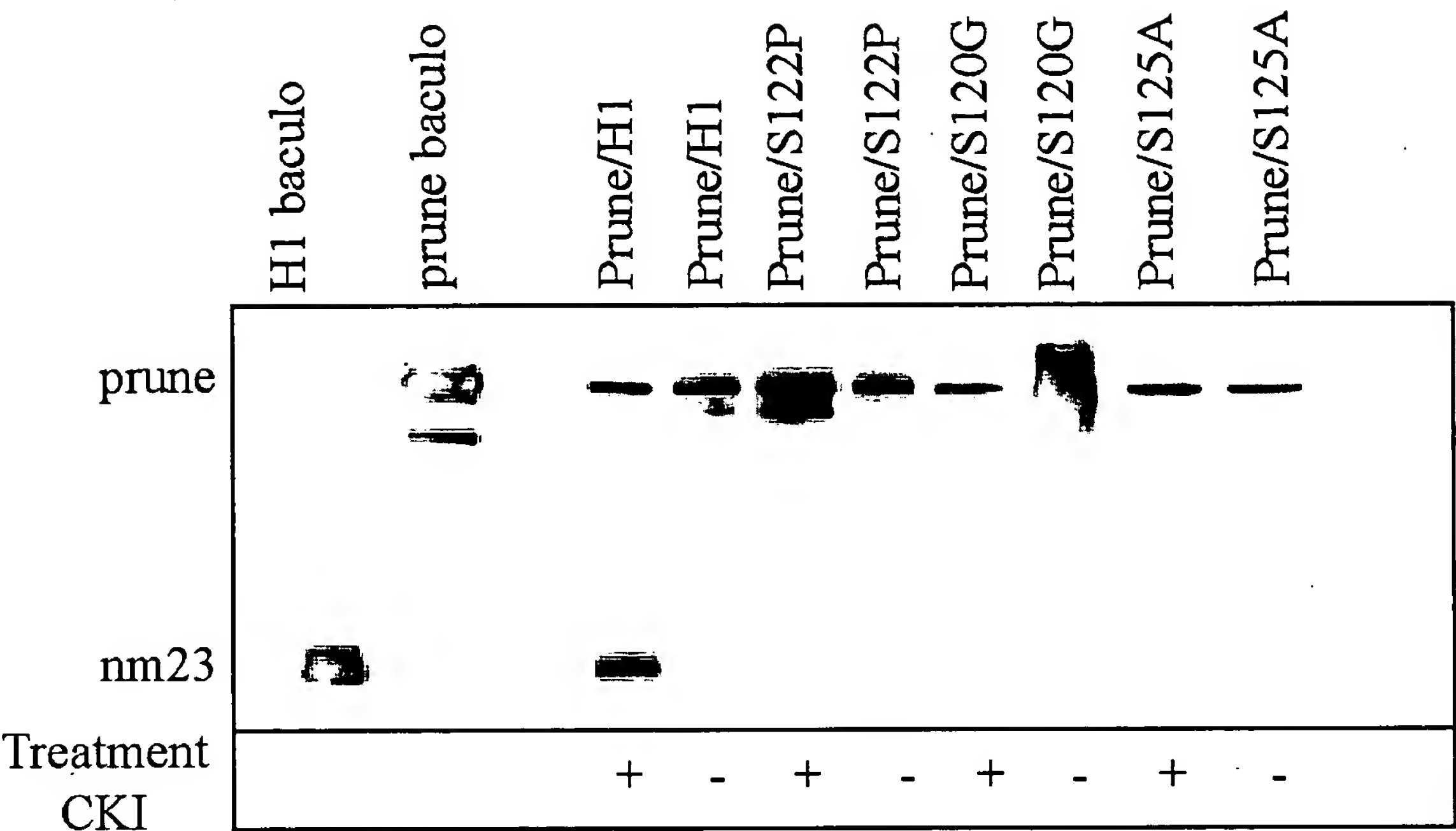
----- h-prune negative  
—— h-prune positive

C)



----- h-prune negative  
—— h-prune positive

**Fig. 10**



A)

MYDVPDYASLGSPVEMA  
NLERTFIAIKPDGVQRGLV  
GEIIKRFEQKGFRLVAMK  
FLRASEEHLKQHYIDLKD  
RPFFPGLVKYMNSGPVVA  
MVWEGLNVVKTGRVML  
GETNPADSKPGTIRGDFCI  
QVGRNIIHGSDSVKSAEK  
EISLWFKPEELVDYKSCA  
HDWVYE

B)

Fig. 11

Voyager Spec #1 MC[BP = 1344,6 21449]

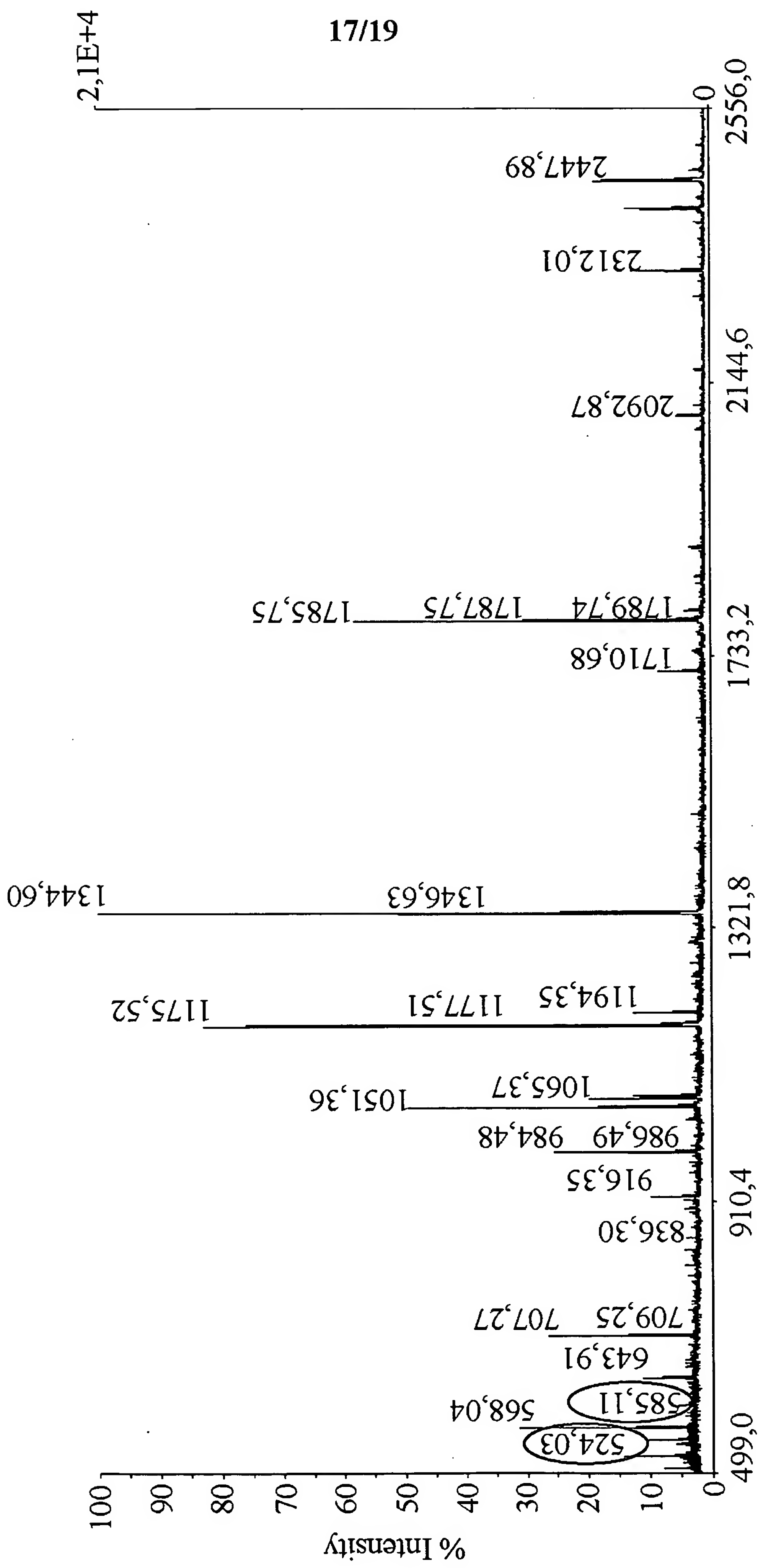








Fig. 11 C

**A**

	1	2	3	4
CKI $\delta$	+	+	-	-
Isoform Nm23	H1	H2	H1	H2

nm23 → 

**B**

IC261	0h	2h	4h	6h	8h	0h
CIP	—	—	—	—	—	+
Phosphorecated nmZH1						
Total nm23H1						

**C**

	1	2	3	4	5
IC261 $\mu$ Mol	—	50	200	—	—

h-prune → 

nm23H1 → 

**Fig. 12**



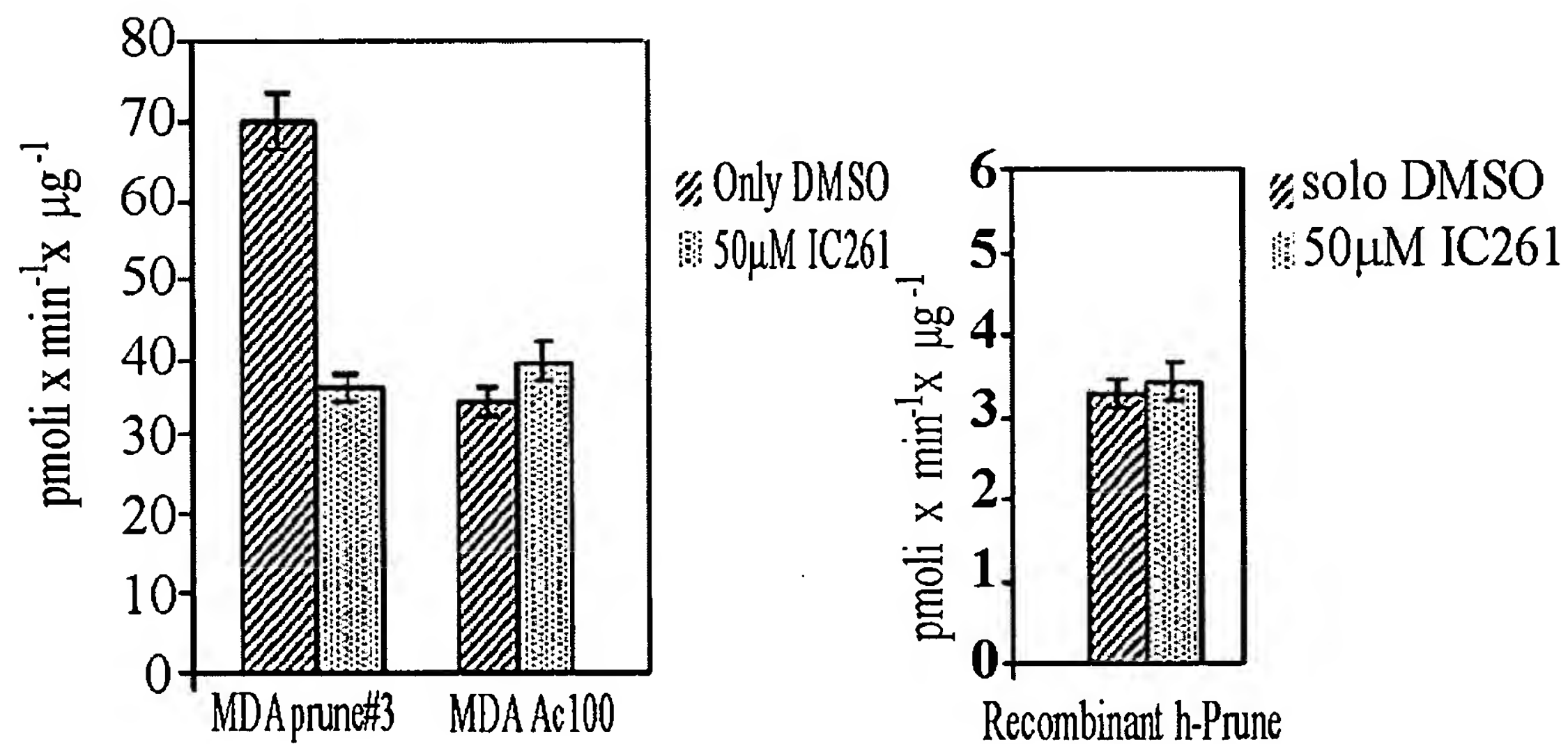
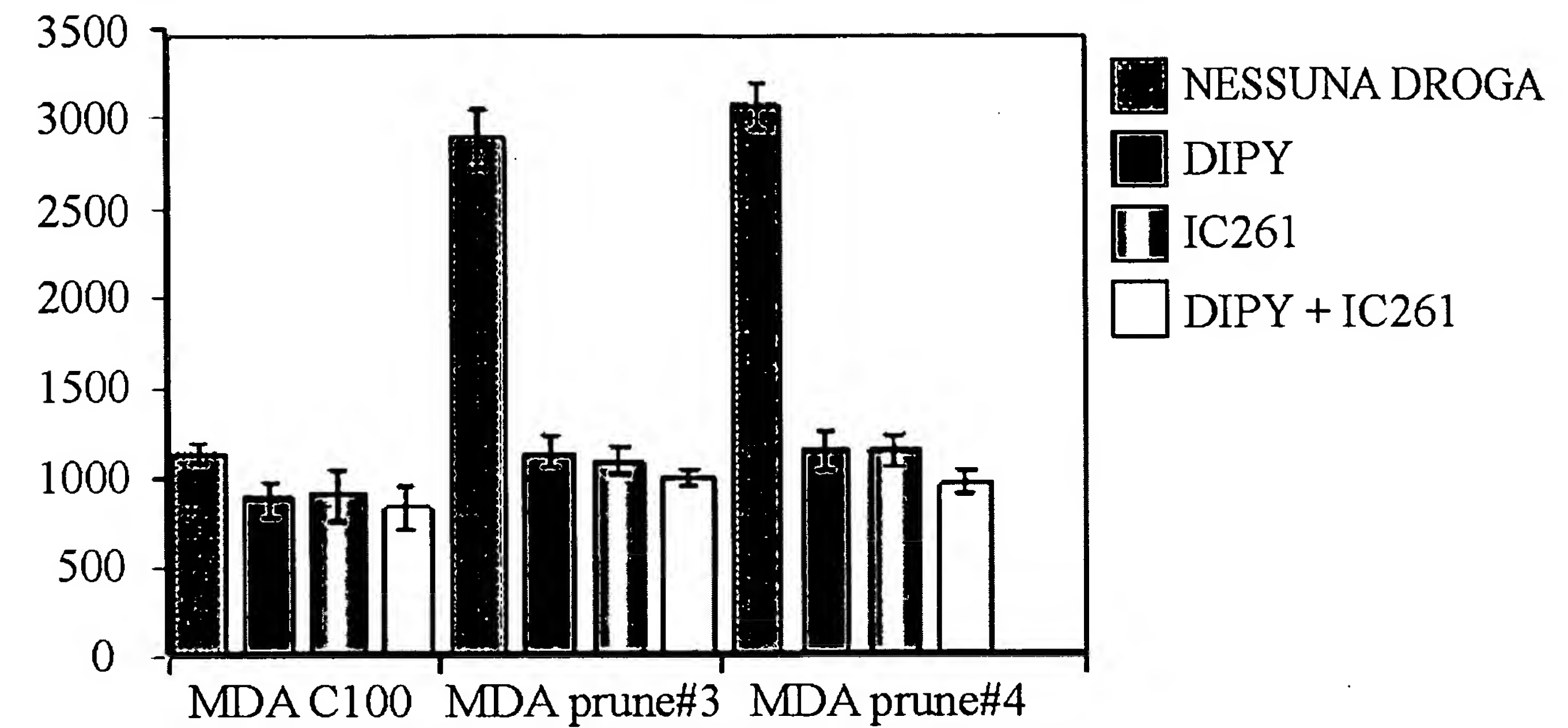


Fig. 13

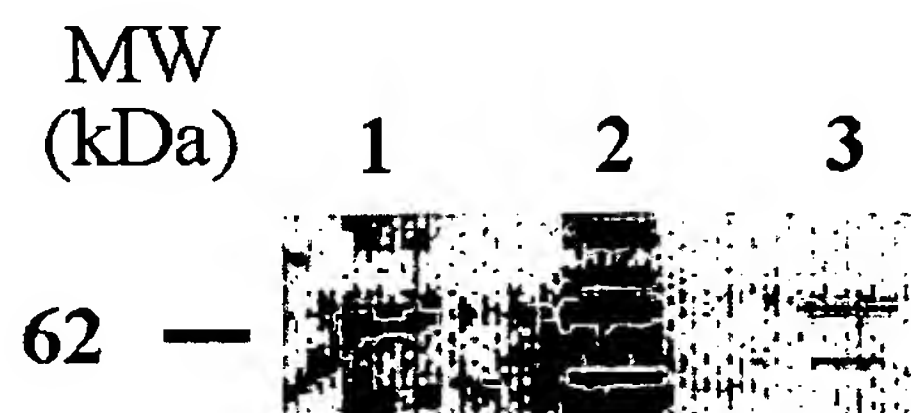


Fig. 14